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THE CLINICAL AND ROENTGENOGRAPHIC MANIFESTATIONS OF PRIMARY ATYPICAL PNEUMONIA, ETIOLOGY UNKNOWN *

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THE increasing prevalence of atypical forms of primary pneumonia in the past decade has been seriously studied both in civilian and military practice throughout North America, Continental Europe and England. A bronchopneumonia similar to the virus pneumonia so common today was probably first described in 1872.[1] Different names have been applied to this syndrome more recently. Beginning in 1934 Gallagher [2] called it "bronchopneumonia"; later, in 1941, the same author [2] named it "acute pneumonitis." Bowen [3] in 1935 demonstrated by roentgenogram an "acute influenza pneumonitis," while Reimann [4] probably first described and named the entity in 1938 "an acute infection of the respiratory tract with atypical pneumonia." In the same year Francis and Magill [5] demonstrated an unidentified virus producing meningitis and pneumonitis in experimental animals. Smiley and associates [6] illustrated in 1939 "an acute interstitial pneumonia," a new disease entity. At this time Stokes and Kenney [7] demonstrated a new filtrable agent associated with respiratory infections. Then in 1940 Kornblum and Reimann,[8] Kneeland and Smetana,[9] Longcope,[10] and Murray [11] independently described this condition.

In 1942 the nomenclature was designated as "primary atypical pneumonia, etiology unknown," by the Commission on Peumonia of the United States Army.[12] Many excellent reports by numerous authors,[13] either in coöperation with the Army or independently, have been presented.

In view of the scarcity of the clinical and physical manifestations in this disease, the roentgenographic examination has been the most substantial aid in the progress of the study of this condition.

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The roentgenographic images produced by the pulmonary lesions of atypical pneumonia have been reported by many authors and on analysis appear to be similar, if not identical. Thus, Seeds and Mazer [14] divide the lesions into three main groups: cotton wool, pseudofibrosis and wire glass.

Bowen [3] and Ackermann [15] have drawn attention to the resemblance of certain cases to tuberculosis, especially when located in the upper lung field. These lesions, however, are not sufficiently characteristic of tuberculosis without the supportive evidence of a period of observation. Kornblum and Reimann,[8] studying cases occurring among medical students and nurses dur-

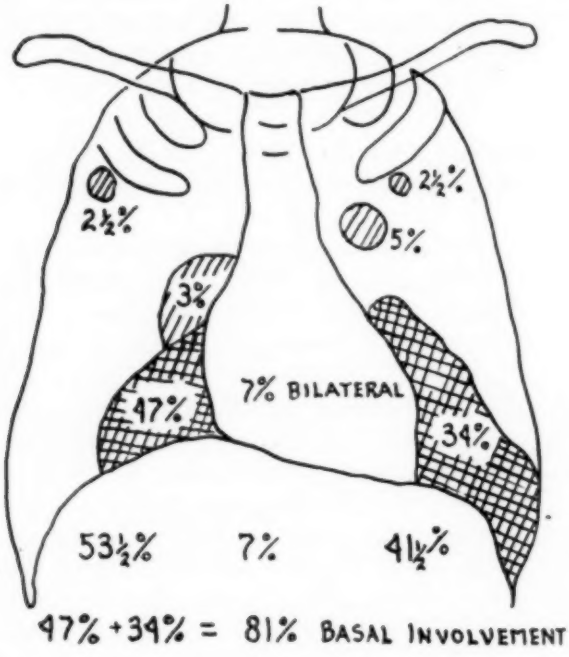


FIG. 1. Diagram representing the percentile frequency of sites of consolidation in a series of 135 cases of primary atypical pneumonia.

ing a mild epidemic of atypical pneumonia, described a picture of acute tracheobronchitis presenting an early stage of this infectious process. They state that the process causes increased density and size of the trunk shadows which are ill-defined and blurred.

From the review of the literature one thing may be clearly noted, i.e., the status of this syndrome has been confusing, and the etiology remains unknown. A clinical study of 75 cases and a radiographic study of 135 cases of primary atypical pneumonia are presented which we feel will aid in the diagnosis of this syndrome.

Etiology. The etiology remains unknown. From four cases Weir and Horsfall [16] isolated a filtrable agent in the mongoose which produced pulmonary lesions, and by passage they were able to demonstrate neutralizing

A B

FIG. 2A. A benign circumscribed atypical pneumonia in the right middle lobe.
FIG. 2B. The roentgenogram of the same patient 6 days later, demonstrating a disseminated focal pneumonia throughout both lungs.

antibodies in the serum of convalescent patients. The apparent resistance of some of their animals to infection, and the failure of serial passage to increase virulence have made the results inconclusive. Eaton and his associates [17] obtained a virus that was pathogenic for the hamster and chick embryo, and the cotton rat. The above results have not been confirmed.

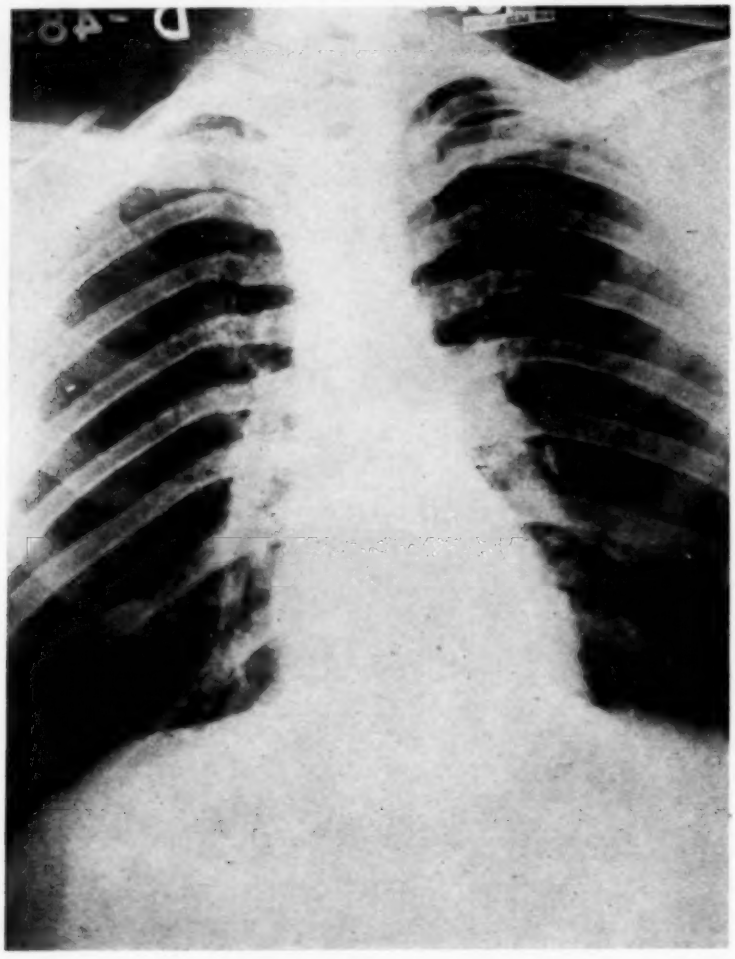
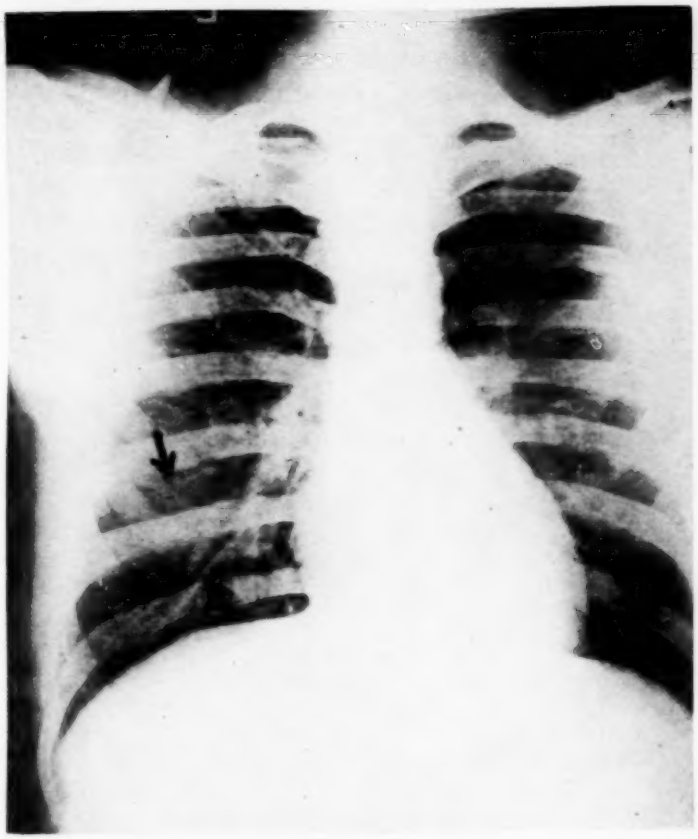


FIG. 2C. The same patient 13 days later with complete resolution.

Epidemiology. Although this condition may have existed well back beyond 1872,[1] we feel the current increase is primarily due to the widespread use of roentgenograms. At least three of our patients were discovered only because they were receiving routine physical examinations and were unaware

FIG. 3A. A 24 year old father with benign circumscribed type of consolidation in the right lower lobe.
FIG. 3B. His 3 year old daughter with a similar consolidation in the same area.
FIG. 3C. His 3 year old daughter with beginning resolution.



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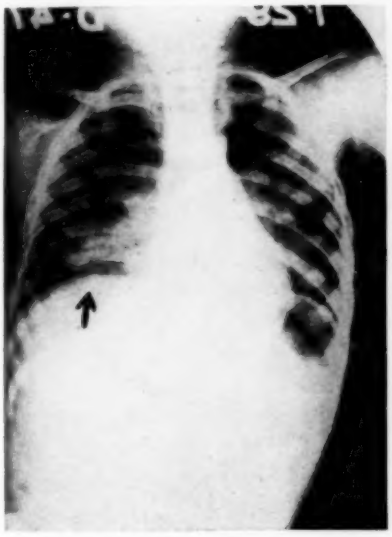

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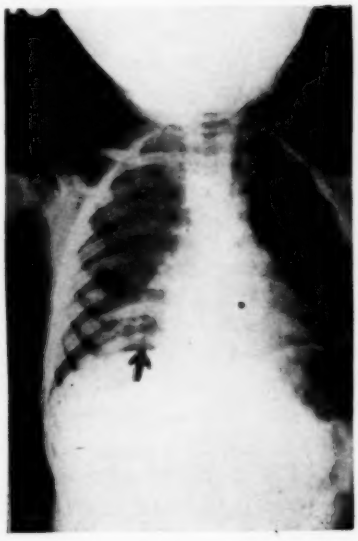

C

FIGS. 3A, 3B, 3C.

of their pneumonic condition, when the examiner, not being satisfied with the chest examination, ordered a routine roentgenogram of the chest. The possibility that sulfonamide therapy has eliminated specific pulmonary infections appears rather questionable, although the sulfadiazine prophylaxis of acute respiratory diseases [18] as recommended by the Army, has reduced the incidence of pneumococcal pneumonia that would follow in the wake of a high rate of acute respiratory diseases. Although it does not appear to be highly contagious, prolonged contacts, such as occur in barracks, college dormitories, and hospitals, have resulted in high incidence of disease, but this may be accounted for by such institutions offering superior controlled studies. Seasonal variation and climate [1] appear to have no influence on the occurrence of this condition.

The age group of our military patients was between 18 and 35 years. There is general agreement that the incidence is high in young adults, as noted in civilian practice by Smith.[19]

Clinical Signs and Symptoms

In an effort to obtain a typical clinical syndrome of primary atypical pneumonia the most frequent symptoms have been tabulated into four groups.

Prodromal symptoms and duration prior to admission to the hospital.

	Percentage of Patients
1. Typical syndrome 1–2 days	47 per cent
2. Pain in chest 2–4 days	40 per cent
3. Previous chest cold and cough 3–10 days	9 per cent
4. No known symptoms	4 per cent

The typical syndrome elicited from 47 per cent of the patients was that of having had a cold from three to 10 days then suddenly developing chills, fever, shortness of breath, cough, headache, sore throat, and generalized aches and pains just prior to admission. The second most common occurrence in 40 per cent of the patients was a history of sharp pain in either side of the chest, or bilateral, aggravated by cough and deep inspiration. Seven per cent in this group had also the symptoms described in Group I. The third group of 9 per cent of the patients gave only a history of about a one to two weeks' duration of a chest cold and moderate cough. The fourth and last group, consisting of 4 per cent of the patients, had no previous history of an upper respiratory infection and were picked up on routine physical examination.

Temperature. The range of temperature varied from normal in three patients, to a maximum temperature of 105.6° F.; the latter was limited to the disseminated focal type of pneumonia (figure 2b). The fever usually subsided in two to five days by lysis. The patients rarely looked as sick as their temperature would indicate.

Pulse and Respiration. The pulse rate usually corresponded to the temperature level. Intense cyanosis with temporary dyspnea was observed in

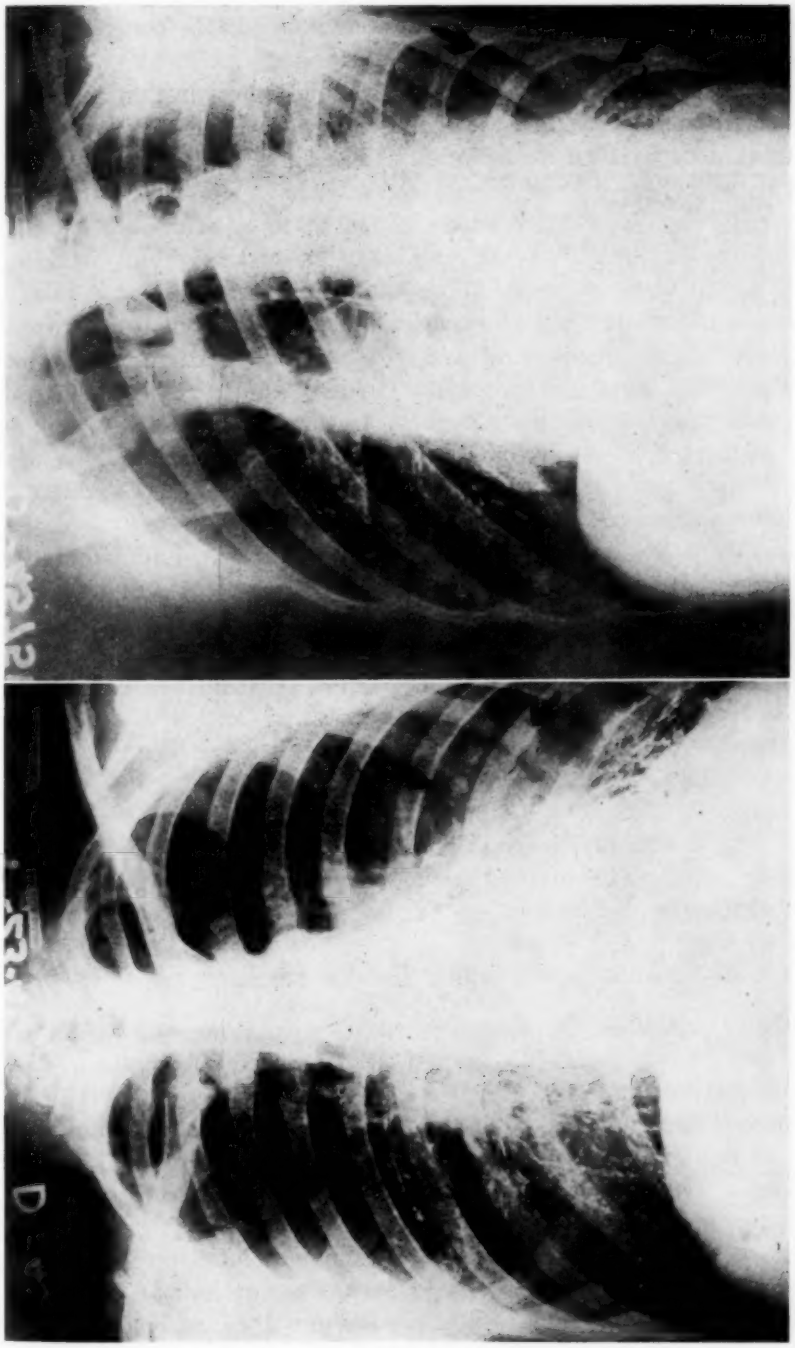

FIG. 4A. Bronchogram illustrating benign circumscribed primary atypical pneumonia of the left pericardial area.

FIG. 4B. Bronchogram illustrating benign circumscribed primary atypical pneumonia of the same case, left oblique projection.

three instances; these patients appeared to have marked relief by oxygen therapy. Asthmatic features were common in about 25 per cent of the patients, occurring commonly when resolution began.

Physical Signs. We concur with Smith [19] and others in the fact that the extent of the lesion disclosed by the roentgenogram was usually greater than that anticipated by physical examination. The signs of frank consolidation were usually absent; râles medium and moist in character were found; mild or moderate dullness and suppression of breath sounds were noted in about 70 per cent of the patients having consolidation. Ramsay and Scadding [20] observed that the association of lobar atelectasis with catarrhal infection produces no acute symptoms, and occurs more frequently than recognized.

Pathology. The fundamental pulmonic lesion is that of an acute interstitial pneumonitis found at necropsy by Golden,[21] similar essentially to that found in influenzal pneumonitis which has been uncomplicated by secondary bacterial invaders or not unlike that seen in measles pneumonitis. The site of the pathologic process is located about the bronchioles and is filled with pus and desquamated cells from the lining as it is partially destroyed. The bronchiolar walls are heavily infiltrated with round cells and lymphocytes, and markedly edematous. There is a lymphocytic infiltration of the alveolar walls in contrast to bacterial pneumonia, whereas the alveolar spaces frequently contain air. Grossly the lungs of primary atypical pneumonia resemble an acute miliary granulomatous process. In the few cases coming to necropsy reported by Kneeland and Smetana,[9] and Longcope [10] the findings were a patchy hemorrhagic interstitial pneumonia associated with bronchitis and bronchiolitis. Grossly there are areas of atelectasis, emphysema, and gray or red consolidation. The bronchi are filled with mucoid or purulent exudate. Microscopically, there is hemorrhagic infiltration of alveoli with mononuclear cells. The alveolar septa may later show thickening with reduction of the alveolar spaces.

Roentgenographic Characteristics

Scadding [22] classifies the pneumonic lesions in primary atypical pneumonia in two main groups: (1) Benign circumscribed pneumonia; (2) disseminated focal pneumonia.

The benign circumscribed variety is fairly well localized, but not sharply defined. It is of uniform density and is located usually in the lower lobes (figure 2a). The disseminated focal type produces pictures of diffuse, rather coarse mottlings, the foci varying from 2 to 5 mm. (figure 2b).

We have found these lesions to be segmental lobular, as have other authors. Only very few cases showed a lobar distribution.

Crysler [23] found that none of the lesions involved an entire lobe even if the posterior anterior view suggested a lobar consolidation. The lateral projection revealed only a part of the lobe as a confluent bronchopneumonia.

Thus an early ill defined localized structural accentuation progresses to a focal or general infiltration and then consolidation.

Aside from other pulmonary conditions this predominantly lobular involvement in atypical pneumonia lends itself to a more convenient morphological and anatomical analysis.

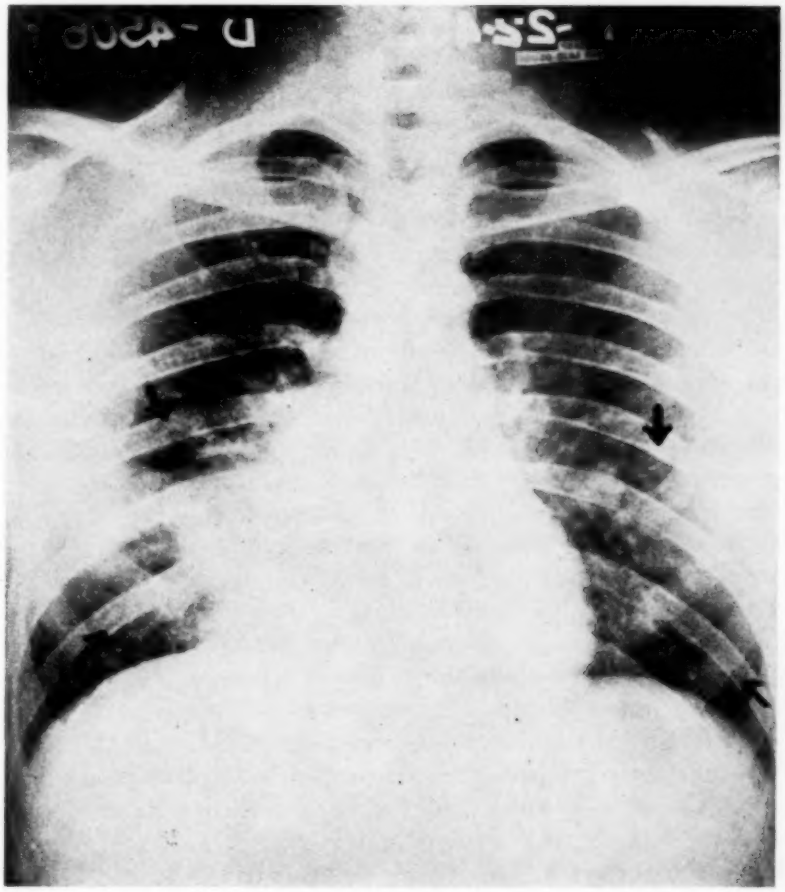

FIG. 5. Benign circumscribed consolidation of right basal lung field and disseminated focal pneumonia left pericardiac area.

Briefly, according to Miller [24] the basic unit of the lung is the primary lobule. It has the form of a truncated pyramid with its base directed toward the periphery of the lung. The primary lobules vary in size from .45 mm. to .845 mm. The larger units are situated in the peripheral and basal portions of the lung. The secondary lobule comprises 50 to 250 of these lobules. Depending upon the size and thickness of the perilobular septum many a structure corresponding with the shape of the lobule can be seen on the normal roentgenogram. In inflammatory conditions the transparent

(black) lobules are surrounded by (gray) increasingly thickened perilobular septa until the lobules disappear, either due to collapse or exudate, thus leading to the picture of consolidation (figures 6a, 6b). The conspicuous feature appears to be the engorgement of the perilobular structures or septa, which is seen in the initial stages and persists around the reilluminated lobule during the resolution of the process.

The resolution is manifested by irregular thinning of the septa, or interstitial tissues, thus enabling the air to be seen again in the lobule (figures 6a, 6b). The condition can be differentiated by increased sharpness of the perilobular septa and reillumination of the lobules. The time of resolution varied with the size of involvement from six days to six weeks usually. The average time of complete resolution did not exceed 16 days.

The differential diagnosis between atypical pneumonia and pulmonary tuberculosis and/or primary pulmonary coccidioidomycosis offers little difficulty in view of the comparatively infrequent involvement of the upper lobes in atypical pneumonia (5 per cent) and the rapidity of resolution of this process. The pulmonary tuberculous lesions present elements of fibrosis, calcification, and exudation due to the chronicity of the lesion. In the review of the cases of primary pulmonary coccidioidomycosis by the authors [25] no calcification of the lesions has been found. The prominent non-calcified hila in primary pulmonary coccidioidomycosis offer another differential diagnostic feature. Laboratory aids are discussed below.

This morphological analysis of the cases is in conformity with the pathological findings and appears to be more adequate than the generally used terms "bronchial" or "peribronchial." The fairly uniform size of the lobule throughout the lungs offers a concrete visible part of the respiratory system in contrast to the diminishing bronchi which cannot be recognized in the periphery without the aid of a microscope. These lobular and perilobular manifestations of the lung are of even greater aid in the differentiation of other pulmonary conditions which are beyond the scope of this paper. The use of the terms "lobular" and "perilobular" seems, therefore, to be indicated in the detailed study of lung pathology.

The basal involvement, consisting of consolidations lodged in the cardiophrenic angle, has been a predominant feature in over 80 per cent of these cases (figures 1, 2a, 3a, 3b, 3c, 4a, 4b). The claim [13] that the ambulatory attitude of the patient may be responsible for the basal manifestation of the disease remains conjectural.

Of the disseminated focal type there were nine cases, or 7 per cent, encountered in the 135 cases (figure 2b). In 47 per cent of the patients the involvement occurred in the right base; in 34 per cent of the patients it appeared in the left base. In 12 patients, or 17 per cent, the upper and middle

FIG. 6A. (*above*) Resolving benign circumscribed type of atypical pneumonia with characteristic lobular and perilobular arrangement in the right cardiophrenic area. (*below*) Mesial lung field: A. Perilobular tissues (septum), gray. B. Secondary lobule, black.

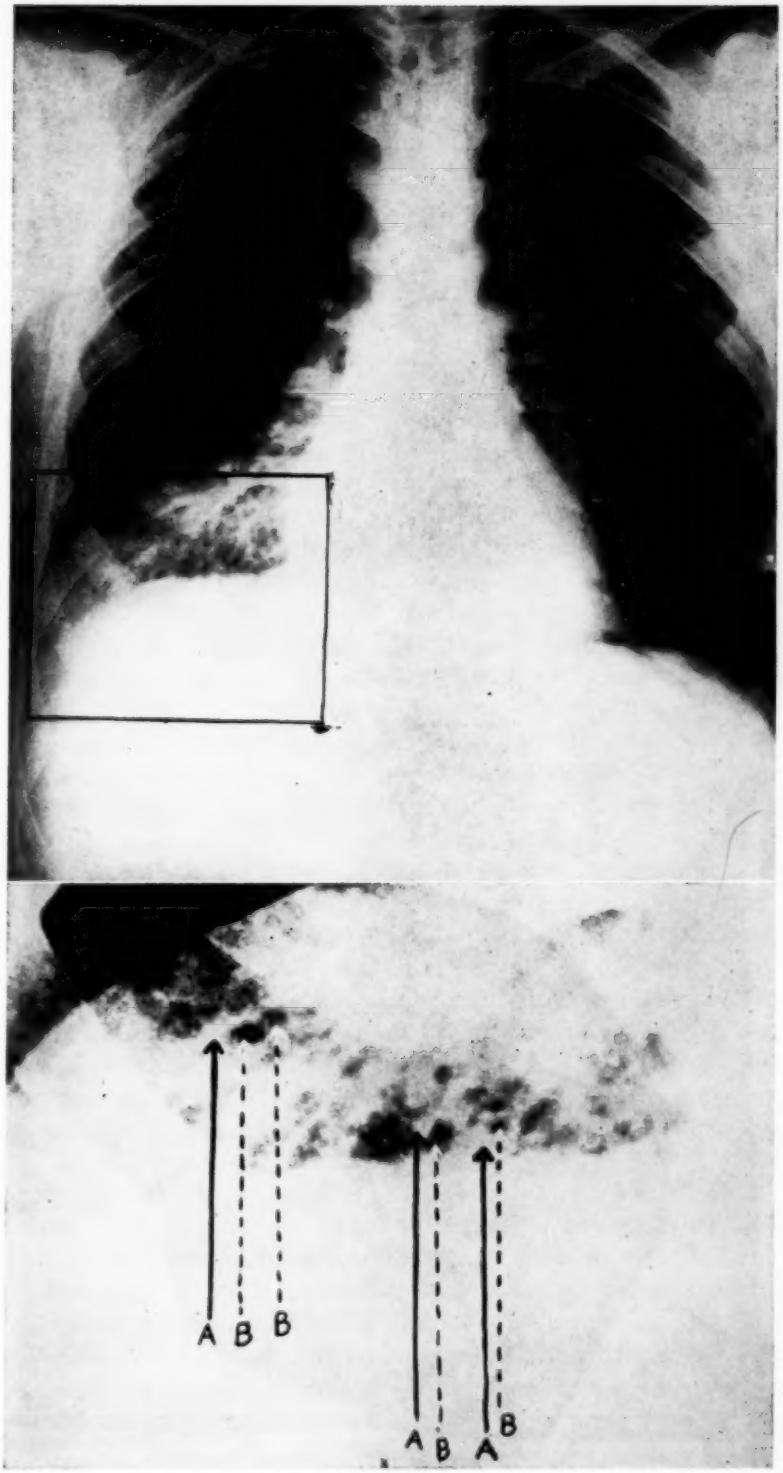

FIG. 6A.

lung fields were involved. Only nine patients developed slight pleural effusion, one a moderate effusion requiring prolonged hospitalization, and three solitary lung abscesses which healed spontaneously.

Laboratory Aids

Sputum. Productive cough with copious sputum was present at the onset in about 30 per cent of the cases, whereas in 70 per cent it started with resolution. Seven patients had blood-streaked sputum at the onset of the illness, but the most common was the mucopurulent type. Sputum smears were made in 95 per cent of the cases. Specific typing sera for pneumococci were employed in each; but only 15 per cent of the cases gave positive Quellung reactions, which invariably were with the high numbered groups. In differentiating pulmonary tuberculosis repeated sputum examinations were required on numerous patients.

Blood. The hematologic studies revealed that the leukocyte count was normal in the majority of cases, as demonstrated in figure 7 showing the initial count in 75 patients. The neutrophiles and monocytes were slightly increased in number, and a lymphopenia was common. Blood cultures were all negative. Leukocytosis was usually associated with secondary bacterial invasion.

Cold Agglutinins. A study of autohemagglutinins or cold agglutinins was made on 12 patients only. They were positive in low titer in eight, positive in high titer in two, and negative in two. Sera were stored before examination, a fact which might account for the low titers. Complement fixation for elementary type of virus was demonstrated in low titer in two of the patients that were negative for cold agglutinins. Repeated blood examinations during convalescence eight to 14 days after onset of illness [26] for demonstration of cold agglutinins were not practicable because of the early recovery of a majority of the cases.

Urine. Transient albuminuria was present only in those patients with high temperatures; hyaline and granular casts were present in a small percentage of these. Blood chemistry remained normal. Transient hematuria was observed in four patients treated with sulfadiazine; uneventful recovery ensued.

Sedimentation Rate. The modified Cutler method of determining the sedimentation rate with a normal of 10 mm. in 60 minutes was employed. Rates were obtained usually on the fourth day after admission. Additional sedimentation rates were taken, and as demonstrated in figure 8 the highest acceleration of the erythrocyte sedimentation test varied considerably in 75 patients. On discharge all patients had a rate less than 15 mm. in 60 minutes. It was found in 10 per cent of the patients that the sedimentation rate

FIG. 6B. (*above*) Identical lobular and perilobular pattern in right costophrenic lung area. (*below*) Peripheral lung field: A. Perilobular tissues (septum), gray. B. Secondary lobule, black.

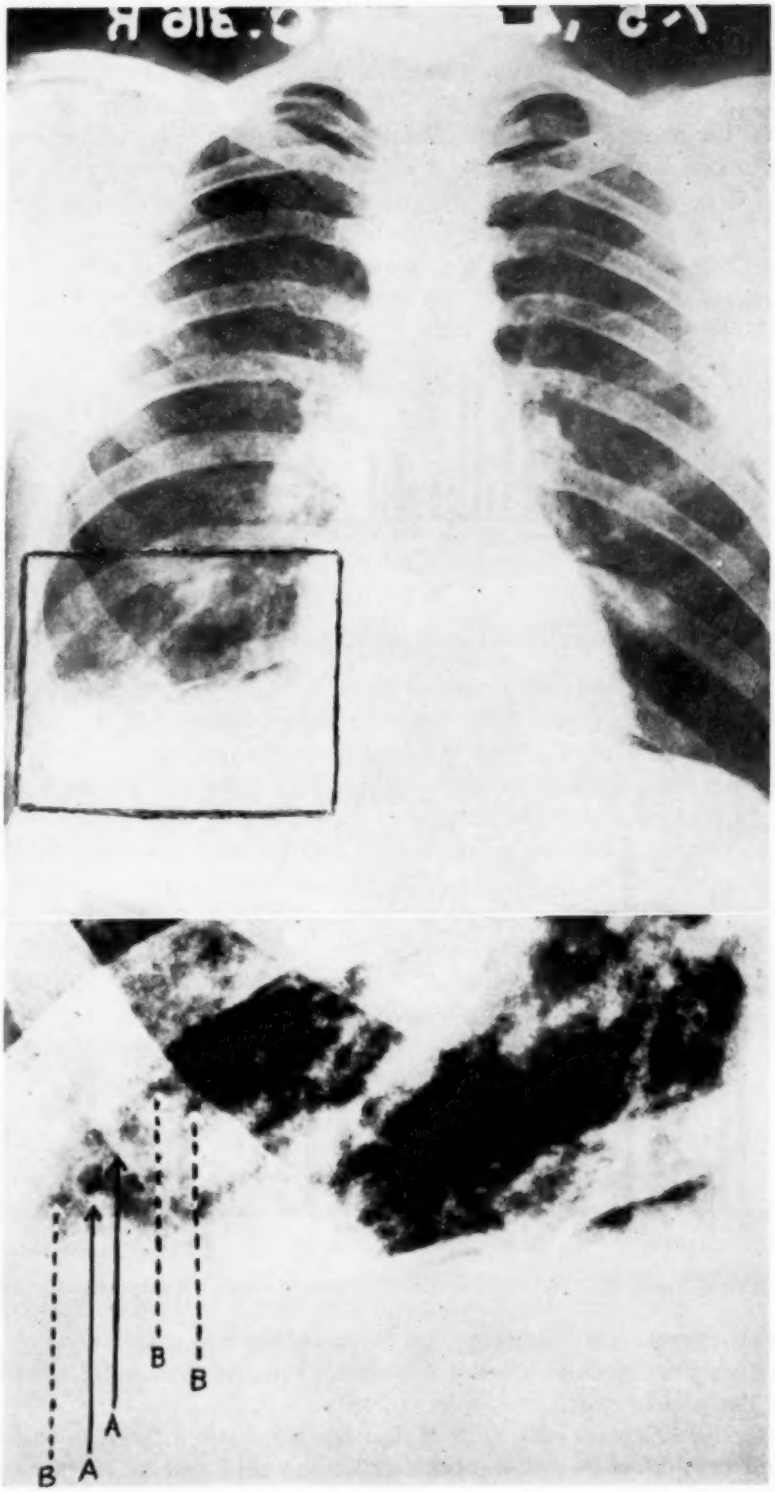

FIG. 6B.

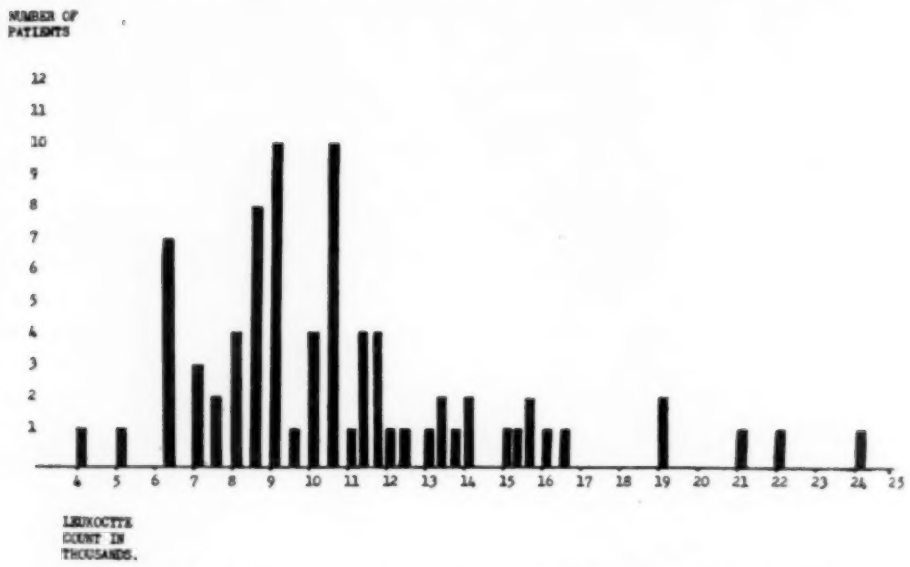

FIG. 7. Initial leukocyte count of 75 patients with primary atypical pneumonia.

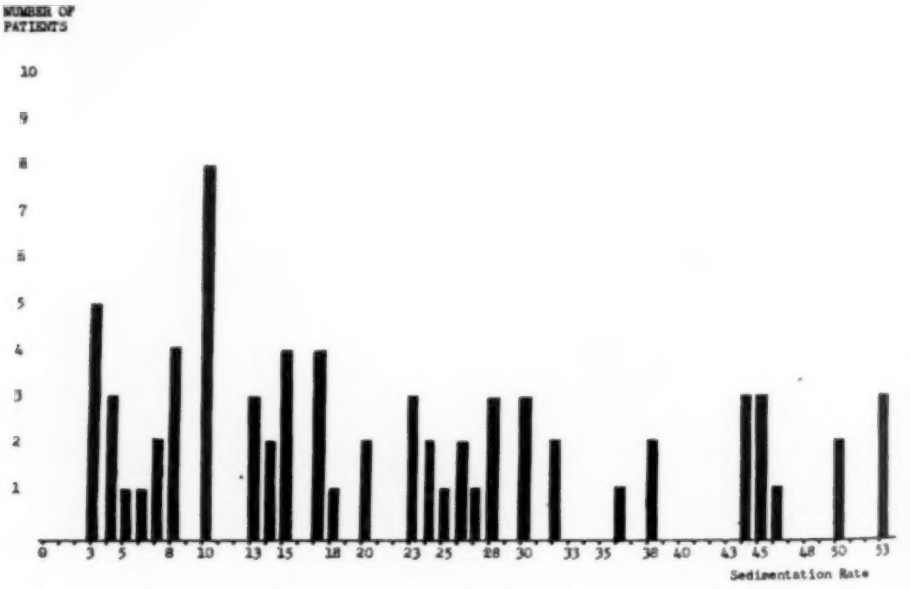

FIG. 8. Highest peak in sedimentation rate of 75 patients with primary atypical pneumonia.

had become normal, although resolution was not complete by roentgenogram. It was also noted that sedimentation rates remained normal in over 21 per cent of the patients with minimum consolidation.

Tuberculin Patch Test. The Vollmer patch test was used in those cases in which resolution was slow or linear lesions persisted by roentgenogram.

The percentage of positive patch tests in this series equaled that found in the general population.

Coccidioidin Skin Test. Coccidioidin skin tests were made on those patients in which resolution was slow, or the hilar distribution was indicative, and on those patients who gave a history of having been in an endemic area. When the tests were positive, reactions of more than 5 mm. in 48 hours,[25] blood precipitin and complement fixation serologic tests were performed by Dr. C. E. Smith of Stanford School of Medicine. No cases of active primary pulmonary coccidioidomycosis were found in these patients.

Complications

Nine patients developed slight pleural effusion, which consisted of mere blunting of the costophrenic angle, and rapidly recovered. One patient developed a moderate effusion which required extensive hospitalization. Three patients developed single lung abscesses, probably from secondary pyogenic invaders; all healed spontaneously with uneventful recovery. No deaths occurred among these patients.

Treatment

So far, treatment has been symptomatic. Oxygen was used liberally where cyanosis and dyspnea were present. Bed rest is essential even in the mildest case. Codeine, throat irrigations, expectorants, steam inhalation, and sedatives are necessary and welcome when the cough is non-productive and painful. Fluids were forced. In uncomplicated cases of primary atypical pneumonia, penicillin and sulfonamides were of no value. Among our patients, penicillin was used in six, and sulfadiazine was used in 18 patients; there was satisfactory response in all. These patients, however, had secondary invasion by pyogenic bacteria, manifested by increasing numbers of pyogenic organisms in the sputum, an abrupt rise in leukocyte count, chills and fever, and usually evidence of roentgenographic spread. Of the six patients treated with penicillin one was sensitive to sulfonamides.

Summary

1. A clinical study of 75 cases and roentgenographic manifestations of 135 cases of primary atypical pneumonia have been described.

2. The salient clinical symptoms were tabulated into four groups.

3. The extent of the pulmonary lesion by roentgenogram is much more extensive than that anticipated by the physical examination, therefore, mild cases may be overlooked if radiographs are not taken.

4. The similarity of primary pulmonary coccidioidomycosis and, to a much lesser degree, pulmonary tuberculosis, requires consideration to avoid error.

5. Roentgenographic manifestations along the more simple "lobular" than hitherto "bronchial" morphology have been postulated and discussed.

6. Normal sedimentation rates are not alone conclusive of complete resolution, therefore, serial roentgenograms will have to be employed.

7. The hematologic studies usually revealed a lymphopenia while the leukocyte count was normal in the majority of cases.

8. The disease has a high morbidity but a low mortality with infrequent complications. In 135 patients, nine developed slight pleural effusions, one of which became moderate requiring prolonged hospitalization; three patients developed solitary lung abscesses which healed spontaneously.

Acknowledgment: We wish to express our appreciation for the photographic aid given by Private First Class Richard H. Dale.

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THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS WITH PENICILLIN: SECOND REPORT *

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New York, N. Y.

In a recent communication [1] the authors reported on the use of penicillin in the treatment of subacute bacterial endocarditis. Of 20 patients in whom the infecting agent was a streptococcus sensitive to the action of the drug, 15 apparently recovered; two were rendered free of infection as long as therapy was continued but subsequently relapsed; three succumbed. In the majority of cases, heparin was employed as an adjuvant to penicillin, but it was felt that further experience was necessary before an opinion could be expressed as to the value of this form of anticoagulant therapy. It was also realized that a further follow-up was desirable in many of the patients who had been observed for only a comparatively short period after treatment had been discontinued.

With the increase in the available supply of penicillin, it became possible to treat by more intensive methods the two patients in the previous series who relapsed after treatment had been discontinued, and to extend treatment to a further series of 15 patients. On the basis of this additional experience an appraisal of the value of heparin has now been made and a regimen is tentatively proposed for the future treatment of patients with this disease. Furthermore, the 15 "recovered" patients in the first series have now been followed for an additional 10 months.

Part I: Results of More Intensive Penicillin Therapy in Two Patients Who Relapsed

In the previous communication it was reported that two patients with subacute bacterial endocarditis (Cases 16 and 17) had relapsed shortly after penicillin therapy was discontinued. Since further intensive treatment provided information of the greatest value in formulating an effective therapeutic regimen for other cases of this disease, the course of this treatment with the results is here presented in detail.

* Received for publication November 23, 1945.

From the Edward Daniels Faulkner Arthritis Clinic of the Presbyterian Hospital and the Department of Medicine, Columbia University, College of Physicians and Surgeons, New York.

The penicillin was provided in part by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council, and in part by Mr. John L. Smith, President of Chas. Pfizer & Company, Brooklyn, N. Y.

† Died April 27, 1945.

Of these two patients, one (Case 16) had received 36,700,000 units in four courses extending over a period of five months; the other patient (Case 17) received 18,390,000 units in four courses over a period of four months. The maximum daily dose which had been administered to the former was 500,000 units and to the latter 320,000 units. Both patients had received heparin for prolonged periods. In spite of their protracted illness and the presence of positive blood cultures when treatment was interrupted, both patients remained in remarkably good clinical condition.

Case 16. O. M. (additional report). On October 15 treatment was resumed. One million units of penicillin were given daily by continuous intramuscular drip for 21 days and the same amount by continuous intravenous drip for a further period of seven days. In addition 4 gm. of sulfadiazine were administered daily. The blood was not heparinized. Penicillin serum levels averaging 0.28 unit per cubic centimeter were maintained throughout. The patient tolerated the procedure remarkably well except for an unexplained episode of pyrexia on the last day of therapy. The temperature gradually returned to normal but there was only moderate subjective improvement and, in spite of frequent transfusions, there was a persistent anemia. For a week after therapy had been discontinued, the temperature remained normal but two days later the blood culture was again positive, and on the same day petechiae were observed. In the succeeding 10 days the temperature gradually rose to 101–102° F., and the clinical condition became worse. Sensitivity tests revealed that, although the infecting strain was perhaps slightly more resistant to penicillin than it had been originally, no striking change had occurred. Accordingly, a further attempt to terminate the infection was made. On November 30 penicillin therapy was resumed and 2,000,000 units were given daily by continuous intramuscular drip for fourteen days. Heparin was not employed. Throughout the period of therapy, the temperature remained between 100–102° F., and there was considerable pain at the site of the infusion. Penicillin serum levels ranged from 0.56 to 4.48 units, usually remaining between 1.12 and 2.24 units per cubic centimeter. After two weeks, treatment was discontinued to permit evaluation of the situation. During the following week the temperature remained below 100° F., blood cultures were sterile, and the patient was allowed up in a wheelchair. On December 22 the patient was discharged. Since then he has continued to be afebrile, and blood cultures have remained sterile. At the time of the last follow-up, August 10, he had gained 16 pounds (7.2 kg.) and had returned to work.

Case 17. M. K. (additional report). On November 9, penicillin therapy was resumed, 500,000 units daily by continuous intramuscular drip. The clinical response was immediately favorable, but on the seventh day the temperature rose to 103.6° F., with intense pain and soreness at the site of injection. Therapy was accordingly discontinued. The clinical course continued favorable, but 12 days later a positive blood culture was again obtained. Five hundred thousand units daily by continuous intramuscular drip were resumed on December 1 and continued for 14 days. During this period the treatment was well tolerated, and the course continued to be quite uneventful until the ninth day after cessation of therapy when the blood culture was again positive. It seemed obvious, therefore, that more intensive therapy was required. Accordingly the patient was permitted to return home on maintenance doses of sulfadiazine until the necessary arrangements could be made for resumption of penicillin therapy. During the first three weeks she remained afebrile and gained 7 pounds (3.1 kg.) in weight, but during the fourth week several minor embolic episodes occurred. On January 29, 1945, she passed a moderate sized embolus to one of the branches of the right posterior tibial artery. On January 30 she was read-

mitted and therapy was resumed, 1,000,000 units daily by continuous intramuscular drip for 12 days. Throughout this period she continued to run an irregular fever, but this was attributed to irritation at the site of the infusion. As soon as penicillin was discontinued, the temperature promptly returned to normal, blood cultures remained sterile, and convalescence proceeded uninterruptedly. The only untoward symptoms have been slight pain, numbness and a tingling sensation in the foot where the embolus occurred. The patient has since married and is leading a normal life.

Discussion of Cases 16 and 17. From the results of therapy in these two cases several points of interest emerge. It was observed that, in difficult cases, maintenance of penicillin serum levels equivalent to twice the amount required to inhibit growth of the infecting streptococcus in vitro might not result in a cure of the patient, even though treatment were continued for as long as four weeks, whereas in both cases intensive therapy with larger daily doses over periods of 14 and 12 days respectively resulted in apparent recovery. Furthermore, although heparin had been used in conjunction with penicillin during the previously unsuccessful courses of therapy, the infection in both patients was eventually terminated by the use of penicillin alone.

As the result of the observation made on the two subjects, it was decided to try shorter and more intensive courses of treatment with penicillin alone in a series of patients.

Part II: Results of Short Intensive Penicillin Therapy in the Treatment of 15 Additional Patients

Selection of Cases. The cases in this group represent consecutive hospital admissions of patients with a diagnosis of subacute bacterial endocarditis. With one exception (Case 30), in every case the infecting organism was a *Streptococcus viridans* or a non-hemolytic streptococcus. Numerous positive blood cultures were obtained before treatment was instituted in all cases. Every patient had murmurs indicative of organic heart disease and most of them showed embolic phenomena, splenomegaly, anemia and microscopic hematuria.

Methods of Penicillin Administration and Course of Therapy. Penicillin was administered for the most part by constant intramuscular drip, either through a No. 19 to No. 22 needle inserted into the quadriceps femoris muscle, or in some cases through a flexible plastic tube [2] similarly inserted into the thigh. In the majority of cases penicillin serum levels were determined daily. A 24 hour volume of 250 to 500 c.c. of penicillin solution in 0.85 per cent sodium chloride was well tolerated whereas larger volumes appeared to cause pain by mechanical distention of the muscle. The site of infusion was usually changed from one thigh to the other every 48 or 72 hours depending on the amount of local reaction, but in some instances an infusion was run continuously into one site for as long as seven days without causing any marked local reaction. The majority of patients, however, complained of slight discomfort in the muscle and many showed mild swelling, redness and heat locally. Although temperatures of 100–102° F.,

apparently caused by reaction to the infusion, were not uncommon during therapy, only once was it necessary to stop treatment because of hyperpyrexia, and there the reaction was apparently due to the particular lot of penicillin used, inasmuch as a subsequent course of therapy by the same route using larger doses of a different lot of penicillin was entirely uneventful.

Blood cultures almost invariably were sterile during therapy, though often the patients continued to look and feel ill. The erythrocyte sedimentation rate remained elevated in the majority of cases until several weeks after cessation of treatment, probably owing in part to the tissue reaction to intramuscular infusion. Major peripheral emboli were uncommon in this group. One patient had a cerebral embolus with hemiplegia during treatment. In one case a small embolus to the cerebrum, resulting in loss of part of the visual field, occurred three weeks after therapy. Blood cultures from this patient have been repeatedly sterile and there has been no evidence of recurrence of the infection during a follow-up period of six months.

Relapses after interruption of therapy have occurred in a number of patients, but it is to be noted that in no case observed to date has the infection recurred later than two weeks after treatment. In no case as yet has the infecting organism developed significant resistance to penicillin even though in one patient (Case 16) relapses occurred repeatedly over a period of six months during which time he was receiving inadequate doses of the drug.

Because the clinical course of these patients under therapy has been so variable, it appears impossible to assess at any time during treatment the success or failure of a particular course of penicillin. It has in fact been necessary to rely upon previous clinical experience in planning a course of treatment and in deciding arbitrarily upon the time to stop. Observation of the patient's general condition and of the blood cultures after cessation of therapy has proved to be the only satisfactory means of determining whether or not further treatment is indicated.

The daily dose of penicillin has varied from 200,000 to 2,000,000 units, depending upon the sensitivity of the infecting organism and upon the serum levels obtained. In general, an attempt has been made to maintain serum penicillin levels at least four times the amount required to inhibit growth of the organism in vitro.

The chief pertinent data relating to these patients are summarized in table 1. Detailed case histories are presented below of 8 patients selected to show the variations in the clinical course encountered in the group.

Case 21. R. L., a woman aged 21, known to have had rheumatic fever, had been admitted 10 weeks previously to another hospital where a diagnosis of subacute bacterial endocarditis was made, 100,000 units of penicillin were administered intramuscularly each day for three weeks with some improvement, but fever recurred when treatment was stopped. On September 1, 1944, she was transferred to the Presbyterian Hospital. On admission she was a frail, delicate, wasted girl, acutely and chronically ill, with fever of 102–104° F., pulse 110–130, mitral stenosis, palpable spleen, clubbed

fingers and painful fingertips. Five blood cultures were positive for *Str. viridans*, which was one quarter as sensitive to penicillin as the standard strain of hemolytic streptococcus (C203 Mv). Starting on September 6, 25,000 units were given every three hours intramuscularly, and on the twelfth day, because a blood culture taken three days previously was positive, the dosage was increased to 40,000 units every three hours. This regimen was continued 13 days more making a total of 6,330,000 units. Heparin was administered subcutaneously, 100 mg. approximately twice a week. Throughout the entire period of therapy the patient failed to show significant improvement. She continued to have an irregular fever, passed numerous small emboli and on several occasions had alarming episodes of paroxysmal tachycardia. Two days after cessation of penicillin the blood culture was again positive and on October 6 therapy was resumed. On this occasion, 300,000 units daily were administered by continuous intramuscular drip. After an initially satisfactory clinical response, organisms were once more recovered in one of two flasks of a blood culture taken on the eleventh day, and about the same time there was a recurrence of low-grade fever. Penicillin was continued for 12 days longer, and since the organism was also sensitive to sulfonamides, sulfadiazine was given during the last seven days. Penicillin was discontinued after 23 days to permit evaluation of the situation. Three days later the patient developed auricular fibrillation and was digitalized. Sulfadiazine was continued for three weeks. In the month following, she remained afebrile and blood cultures were sterile. She continued to gain in strength, the erythrocyte sedimentation rate returned to normal, and on December 1 she was discharged to a convalescent home.

During the following six months the patient remained free from signs or symptoms of infection, although she had a marked decrease in cardiac reserve. Blood cultures taken on January 29 and March 30 were sterile and the sedimentation rate remained normal. On May 28 she complained of pain in the cardiac area, but had no other symptoms. The following morning she was found dead. An autopsy was performed eight hours later. The cause of death was not determined but the heart was greatly enlarged and showed severe mitral stenosis. On the mitral valve were several small vegetations which on microscopic section showed no bacteria and no acute inflammatory reaction. Although a *Streptococcus viridans* was cultured from the heart's blood at post mortem eight hours after death, it appeared to be different from the strain recovered from the blood during the patient's illness. The postmortem strain grew in the form of large, smooth, grayish-white colonies on blood agar and produced diffuse clouding in liquid medium. The original strain, on the other hand, produced small matt colonies on blood agar and a coarsely granular type of growth in broth. Rabbit antiserum prepared with the original strain and containing agglutinins in high titer against this strain failed to agglutinate the organism recovered at autopsy. Furthermore, the postmortem strain was 10 times as sensitive to penicillin as the original organism. It was therefore concluded that the patient had been cured of the infection and that the organism grown from the heart at autopsy was either a contaminant or represented a postmortem invasion of the blood.

Case 24. W. B., a man aged 33, known to have had rheumatic fever at the age of 7 with several recurrences in succeeding years, began to have easy fatigability, vague pains and anorexia in July 1944. In the following two months he lost 10 pounds in weight, had fever and noticed painful fingertips. On admission September 18, he had conjunctival petechiae, mitral and aortic rheumatic heart disease, palpable spleen and clubbed fingers. *Str. viridans*, twice as sensitive to penicillin as the standard strain, was cultured from the blood. Penicillin therapy was started on September 29, 200,000 units daily by constant intramuscular drip for 21 days. Heparin was not employed. After the third day of therapy, blood cultures were sterile and the temperature remained below 100° F. The erythrocyte sedimentation rate dropped

TABLE I

The Treatment of 17 Cases of Subacute Bacterial Endocarditis with Penicillin

Case No.	Pt. Age Sex	Primary Cardiac Disease	Probable Duration of Infection	Infecting Organism		Penicillin				Average Blood Level, U/c.c.	Result	Follow-up 9/1/45
				Type	Sensitivity to Penicillin, Units per c.c.*	Dates of Therapy	Dose in Units and Route	No. Days	Total per Course and per Patient			
16	O. M. M–30	Rheum. aortic and mitral	7–8 mos.	*Strep. vir.*		a, b, c, d[1]		**103**	**36,700,000**[1]			
					0.14	(e) 10/15/44–11/11/44	1,000,000 IM drip or IV drip	**28**	**28,000,000**	.28		
					0.28	(f) 11/30/44–12/14/44	2,000,000 IM drip	**14**	**28,000,000**	1.12	Recov.	8 mos.
								145	92,700,000			
17	M. K. F–21	Rheum. mitral	7 mos.	*Strep. vir.*		a, b, c, d[1]		**85**	**18,390,000**[1]			
					0.035	(e) 11/ 9/44–11/16/44	500,000 IM drip	**7**	**3,500,000**	.14		
					0.07	(f) 12/ 1/44–12/14/44	500,000 IM drip	**14**	**7,000,000**	.28		
					0.07	(g) 1/30/45– 2/10/45	1,000,000 IM drip	**12**	**12,000,000**	.56		
								118	40,890,000		Recov.	7 mos.
21	R. L. F–21	Rheum. mitral	3 mos.	*Strep. vir.*	0.07	(a) 9/ 6/44– 9/30/44	25–40,000 q3h IM	**24**	**6,330,000**			
					0.2	(b) 10/ 6/44–10/28/44	300,000 IM drip	**23**	**6,900,000**	.14		
								47	13,230,000		Died†	
22	E. B. M–45	Rheum. aortic	3½ mos.	*Strep. vir.*	0.035	9/16/44–10/ 7/44	300,000 IV drip	22	6,600,000	.07	Recov.	11 mos.
23	W. D. M–35	Rheum. aortic	2 wks.	*Strep. vir.*	0.035–0.017	9/22/44–10/13/44	200,000 IV drip	21	4,300,000	.03	Recov.	11 mos.
24	W. B. M–33	Rheum. mitral	3 mos.	*Strep. vir.*	0.008	9/29/44–10/20/44	200,000 IM drip	21	4,200,000	.03	Recov.	10 mos.

* Sensitivity of *Str. hemolyticus* C203Mv = 0.017 U/c.c.

TABLE I—*Continued*

Case No.	Pt. Age Sex	Primary Cardiac Disease	Probable Duration of Infection	Infecting Organism		Penicillin				Average Blood Level, U/c.c.	Result	Follow-up 9/1/45
				Type	Sensitivity to Penicillin, Units per c.c.*	Dates of Therapy	Dose in Units and Route	No. Days	Total per Course and per Patient			
25	S. M. M–36	Rheum. aortic and mitral	5 wks.	*Strep. vir.*	0.14–0.28 0.14–0.28 0.28	(a) 11/ 1/44–11/10/44 (b) 11/30/44–12/11/44 (c) 12/29/44– 1/11/45	500,000 IM drip 500,000 IM drip 1,000,000 IM drip	10 10 14	5,000,000 5,000,000 14,000,000	.14 .28 .56		
								34	24,000,000		Recov.	8 mos.
26	H. G. M–42	Congen. patent ductus arter.	8½ mos.	*Strep. vir.*	0.035	11/20/44–11/29/44	500,000 IM drip	10	5,000,000	.14	Recov.	9 mos.
27	R. J. M–21	Rheum. aortic and mitral	6 wks.	*Strep. vir.*	0.017	12/ 1/44–12/10/44	200,000 IM drip	10	2,000,000	.07	Recov.	9 mos.
28	J. G. M–28	Rheum. aortic and mitral	3 mos.	*Strep. vir.*	0.07	12/13/44–12/22/44	500,000 IM drip	10	5,000,000	.28	Recov.	8 mos.
29	H. B. M–51	Rheum. mitral	9 mos.	Indiff. Strep.	0.035	12/29/44– 1/ 8/45	500,000 IM drip	10	5,000,000	.56	Recov.	8 mos.
30	M. M. M–16	Congen. ? type	19 mos.	Micro-aerophilic micro-coccus	approx. 0.017	1/18/45– 1/27/45	500,000 IM drip	10	5,000,000	.28	Recov.	7 mos.
31	H. L. M–59	Congen. vent. septal defect	6 wks.	*Strep. vir.*	0.035–0.017	2/26/45– 3/ 7/45	500,000 IM drip	10	5,000,000	.2	Recov.	6 mos.

TABLE I—*Continued*

Case No.	Pt. Age Sex	Primary Cardiac Disease	Probable Duration of Infection	Infecting Organism		Penicillin				Average Blood Level, U/c.c.	Result	Follow-up 9/1/45
				Type	Sensitivity to Penicillin, Units per c.c.*	Dates of Therapy	Dose in Units and Route	No. Days	Total per Course and per Patient			
32	M. B. F–13	Congen. ? vent. septal defect	5 mos.	Indiff. strep.	0.017	(a) 3/ 5/45– 3/13/45	200,000 IM drip	7	1,400,000	.03		
						(b) 3/22/45– 4/ 1/45	500,000 IM drip	10	5,000,000	.2		
						(c) 4/16/45– 4/29/45	1,000,000 IM drip	14	14,000,000	.4		
						(d) 5/15/45– 6/11/45	500,000 IM drip	28	14,000,000	.2		
								59	34,400,000		Recov.	3 mos.
33	E. A. M–50	Rheum. aortic and mitral	7 mos.	Indiff. Strep.	0.035	3/26/45– 4/ 7/45	500,000 IM drip	13	6,500,000	.4	Died†	
34	E. P. F–37	Rheum. mitral	6 mos.	*Strep. vir.*	0.07	(a) 4/ 6/45– 4/19/45	500,000 IM drip	14	7,000,000	.2		
						(b) 4/29/45– 5/ 5/45	25,000 q3h IM (operation)	6	1,150,000			
								20	8,150,000		Recov.	4 mos.
35	O. B. F–23	Congen. patent ductus arter.	9 mos.	*Strep. vir.*	0.035	4/13/45– 5/ 1/45	500,000 IM drip	19	9,500,000	.2	Recov.	4 mos.

† Died of heart failure. No evidence of active infection at autopsy.

from 63 to 14 mm. in one hour, and on November 12 the patient was discharged to convalesce at home. Since then he has resumed his occupation as an office worker and has remained entirely free of symptoms. Repeated blood cultures have been sterile.

Case 25. S. M., a man aged 36, had polyarthritis at the age of 16 followed by questionable cardiac involvement. He had previously been admitted to another institution where blood cultures revealed *Str. viridans* and penicillin therapy had been instituted, 100,000 units daily for 10 days. There had been a temporary response, but after cessation of therapy, symptoms recurred and blood cultures were again positive. On Oct. 22, 1944 he was admitted to the Presbyterian Hospital with malaise and fever of four weeks' duration. Physical examination revealed fever, mitral and aortic rheumatic heart disease, palpable spleen and petechiae on the finger tips. Four blood cultures were positive for *Str. viridans,* and the organism was one-eighth to one-sixteenth as sensitive to penicillin as the standard strain. Penicillin therapy was started on November 1, 500,000 units daily by intramuscular drip and continued for 10 days. The temperature response was prompt; blood culture became sterile on the third day and remained so throughout the period of treatment. Although the patient continued to be asymptomatic, a blood culture taken four days after cessation of therapy was again positive and shortly thereafter there was a recrudescence of fever. Blood cultures remained positive in the two succeeding weeks and on November 30 penicillin was resumed. Five hundred thousand units were again given daily by intramuscular drip and therapy was continued for 10 days. Throughout this period, the temperature remained normal but the day following discontinuation of treatment, it rose to 103° F. and the blood culture was again positive. Although in vitro tests showed that there was no significant change in the penicillin sensitivity of the infecting strain, the evidence strongly suggested that the infection could not be terminated by the dosage of penicillin which was then available. The patient was therefore placed on maintenance doses of sulfadiazine and allowed to return home for Christmas. In the meantime, a supply of penicillin permitting more intensive therapy became available. The patient was accordingly readmitted on December 29 and immediately started on 1,000,000 units daily by continuous intramuscular drip. Heparin was not employed. Therapy was continued for 14 days. The blood culture was sterile on the fifth day and remained so thereafter. During the first week the temperature remained below 100° F. but rose to 103° F. during the second week and on the fourteenth day reached 105° F. However, there were no associated symptoms and it was concluded that the febrile response was due to local irritation from the intramuscular drip. When therapy was discontinued, the temperature promptly fell and the erythrocyte sedimentation rate gradually returned to normal; blood cultures remained sterile and the patient continued to be asymptomatic. He was discharged on February 6 apparently in excellent health. At the time of the last follow-up visit seven months after cessation of therapy, the blood culture was sterile and there was no evidence of a recurrence of the infection. He has since returned to full time office work, looking the picture of health.

Case 28. J. G., a man aged 28, known to have had several attacks of rheumatic fever and chorea in childhood, was admitted on Dec. 1, 1944 with fever, loss of weight and energy in the preceding two and a half months. Examination revealed mitral and aortic valvular disease, palpable spleen, conjunctival petechiae and temperature of 101–104° F. Four blood cultures yielded *Str. viridans,* one-quarter as sensitive to penicillin as the standard strain. Penicillin was started on December 13, 500,000 units daily by constant intramuscular drip, and continued for 10 days. Heparin was not employed. Except for a rise to 101.8° F. on one occasion the temperature remained normal throughout. Blood cultures at the termination of therapy and at weekly intervals thereafter were sterile. The patient gained 10 pounds (4.5

kg.) in weight while in the hospital and the erythrocyte sedimentation rate gradually fell to normal. He was discharged on Jan. 11, 1945 feeling extremely fit. Since then he has been working full time as an accountant and regular follow-up examinations have shown no evidence of a recurrence of the infection.

Case 29. H. B., a man aged 51, had had low-grade fever, fatigue, migratory pains, weight loss and malaise since April 1944. There was no history of rheumatic fever or heart disease. He had continued to work as a bookkeeper until October 27 when he was suddenly seized with severe substernal pain and admitted to the hospital two hours later. Examination revealed classic signs of anterior myocardial infarction and he was placed on the usual coronary regimen for four weeks. During this period the white blood cell count returned to normal, but the temperature and erythrocyte sedimentation rate remained elevated and he continued to feel ill. There was a systolic murmur at the apex, the spleen was palpable and the fingers clubbed. During the sixth week embolic phenomena were observed on the left middle finger and in the fundus of the right eye. Blood cultures, which had hitherto been reported sterile, revealed an indifferent streptococcus on four occasions. The organism was one-half as sensitive to penicillin as the standard strain. On December 29 penicillin was started, 500,000 units daily by intramuscular drip, and continued for 10 days. During the first week of therapy, there was a favorable response in temperature and great subjective improvement. During the last three days a recrudescence of fever occurred which was interpreted as a reaction to the intramuscular penicillin. Throughout the period of treatment the patient continued to have drenching night sweats, the erythrocyte sedimentation rate remained rapid, the white blood cell count was slightly elevated, and he passed several small emboli to the upper extremities. In spite of these ominous signs, therapy was discontinued on the tenth day. In the following three weeks he continued to improve and to gain weight; the temperature gradually returned to normal, night sweats ceased, the erythrocyte sedimentation rate fell from 115 to 45 mm. in one hour and five blood cultures were sterile. He was discharged on Feb. 2, 1945, three and a half weeks after cessation of therapy, in good general condition. The patient has now returned to his work and is in excellent health. Blood cultures taken at monthly intervals have all been sterile.

Comment: The patient continued to pass emboli and had fever, leukocytosis and a rapid erythrocyte sedimentation rate after the infection had apparently been controlled. Similar observations have been noted in several other patients.

Case 30. M. M., a youth aged 16, had been followed in the Pediatrics Cardiac Clinic since the age of 6 because of congenital heart disease, thought to be due either to an interventricular septal defect or patent ductus arteriosus. The past history included a transient cerebral episode with hemiplegia at the age of 6, bronchitis and bronchial asthma at the age of 12 and primary atypical pneumonia at 14. In June 1943 he was admitted to the hospital with malaise, fever and night sweats. There was a loud harsh systolic murmur with thrill over the mid-sternum. No petechiae were observed and the spleen was not palpable. For 10 weeks he continued to run an irregular fever which responded temporarily on two occasions to sulfadiazine. Although blood cultures on eight occasions were reported sterile, the consensus of opinion was that he had subacute bacterial endocarditis and he was discharged on maintenance doses of sulfadiazine. During the following 15 months he continued to run an intermittent fever and had several episodes suggesting pulmonary infarction. The spleen was also palpable. His general condition, however, remained remarkably good and in August 1944 he was readmitted for further study. A non-hemolytic micrococcus was isolated from the blood on two occasions but numerous other cultures were sterile. Blood respiratory gas studies carried out after catheterization of the right heart made the presence of an interventricular septal defect appear unlikely and exploration for patent ductus arteriosus was performed. At operation a patent ductus

could not be demonstrated. The subsequent course of the disease was essentially unchanged. The patient continued to run an intermittent fever with occasional episodes suggesting pulmonary infarcts. Dyspnea on exertion increased but he continued to be up and about. On Jan. 11, 1945 he was readmitted for further study and possible penicillin therapy. A low-grade fever persisted and on four occasions a slow-growing microaerophilic micrococcus was isolated from the blood. The organism was sensitive to penicillin but the exact degree of sensitivity could not be determined with accuracy. Penicillin therapy was started on January 18, 500,000 units daily by intramuscular drip, and continued for 10 days. The subsequent course was uneventful. The temperature remained below 100° F., the erythrocyte sedimentation rate fell from 50 to 5 mm. in one hour and blood cultures were sterile. Therapy was discontinued on January 28 and the patient was discharged on February 8, completely asymptomatic. At the time of the last follow-up visit he continued to look the picture of health and blood cultures remained sterile.

Case 32. M. B., a girl aged 13, was admitted Feb. 26, 1945 with the complaint of recurrent chills and fever of five months' duration. A heart murmur had been recognized since infancy and there was no history of rheumatic fever. Symptoms of chills and fever had been present since September 1944 with daily rises in temperature to 103° F. for the past month. During the last 10 days there had been showers of petechiae. Sulfonamides, 2 gm. daily, had been administered on several occasions with but temporary relief of symptoms. Physical examination revealed a temperature of 102.3° F., the appearance of chronic illness, a palpable spleen and several petechiae. The heart was not enlarged, but in the fourth interspace to the right and left of the sternum there was a harsh systolic murmur thought to be due to an interventricular septal defect. Blood cultures on four occasions revealed an indifferent streptococcus which was equally as sensitive to penicillin as the standard strain. Therapy was started on March 5, 200,000 units of penicillin daily by constant intramuscular drip for seven days. Four days after stopping treatment the temperature was normal and blood culture sterile, but in four more days the fever recurred and blood culture was positive. A second course of penicillin, 500,000 units daily for 10 days was started on March 22. The clinical response was again excellent, and serum levels of penicillin averaged 0.2 unit per cubic centimeter. However, nine days after therapy, fever and a positive blood culture reappeared, the organism having the same sensitivity as it had had originally. Accordingly, 14 days after the second course, a third period of treatment was undertaken, this time 1,000,000 units for 14 days. Serum levels of penicillin averaged 0.4 unit per cubic centimeter. Low-grade fever persisted during this course, apparently caused by the intramuscular drip, for the temperature fell to normal 24 hours after cessation of therapy. The blood culture was sterile five days later, but on the ninth and twelfth days, although there were no clinical signs of relapse, growth was again obtained. The organism was still equally as sensitive to penicillin as the standard strain.

Although her clinical condition remained excellent, it was clear that this patient was unusually refractory to treatment. It was therefore decided to try a more prolonged course of therapy. Accordingly, she was given four weeks of continuous intramuscular penicillin, 500,000 units daily starting on May 15. The response to this fourth course appears to have been satisfactory. The patient has had consistently negative blood cultures and has been sent home free from symptoms.

Case 33. E. A., a man aged 50, had rheumatic fever in 1919 and a heart murmur thereafter. In August 1944 he noticed fever and weight loss. Blood cultures at another hospital revealed an indifferent streptococcus and he was given penicillin, 20,000 units every two hours intramuscularly for two courses totalling 3,500,000 units each. Blood cultures became negative during therapy, but growth was again obtained one week after each course.

He was admitted to the Presbyterian Hospital on March 24, 1945. Physical examination revealed a chronically ill male with clubbed fingers and a palpable spleen. The heart was enlarged and overactive with loud aortic systolic and diastolic murmurs. Blood cultures revealed an indifferent streptococcus which was one-half as sensitive to penicillin as the standard strain. Penicillin was administered starting on March 26, 500,000 units daily by constant intramuscular drip for 13 days. Blood culture was sterile on the fourth day and eight different cultures taken before his death remained so. On the third day of therapy the patient developed a left total hemiplegia probably due to embolization of the right middle cerebral artery. Following this he ran a downward course, developed cardiac failure, bronchopneumonia and severe cachexia. He died two and a half months after therapy was stopped. At autopsy he was found to have complete rupture of one aortic cusp and several elongated vegetations on the mitral valve. Postmortem heart's blood was sterile in two flasks. Ground up bits of vegetation which had been taken without aseptic technic cultured only *B. subtilis* and gram negative rods. Microscopic sections of the vegetations showed no bacteria.

In this case, although the infection was controlled, the patient died from complications of the disease.

Summary of Results and Discussion. Of the 15 additional cases reported, the infection appears to have been terminated in every instance. One patient (Case 21) died suddenly seven months after therapy and at autopsy was found to have no evidence of persisting infection. One patient (Case 32) has relapsed repeatedly but at present appears to be bacteria-free two months after therapy. In one further instance (Case 33) the infection was controlled but the patient died of cardiac failure two and a half months after therapy. Ten of the 15 patients have already returned to full activity.

It is noteworthy that of 11 patients treated for periods of 14 days or less, the infection was terminated in all but one instance. In every case the serum level maintained was at least two to four times the amount necessary to inhibit the organisms by our in vitro test. In some patients the rôle of previous courses of penicillin in the ultimately favorable result is difficult to evaluate. It is possible that partial healing of vegetations had already taken place although complete sterilization had not occurred as a result of previous treatment. However, in 6 cases in which a single course of 10 days' duration was the only penicillin received, the infection appears to have been terminated as judged by follow-up periods varying from six to nine months.

Part III: An Appraisal of the Rôle of Heparin in the Treatment of Bacterial Endocarditis

The use of heparin combined with penicillin in the treatment of bacterial endocarditis has been advocated by Loewe [3] and others. In their previous report the authors [1] have discussed their experiences with heparin in 15 cases and expressed the opinion that it was of doubtful value. The effect of penicillin alone as observed in 12 additional cases reported herein offers further evidence that heparin is not essential in the treatment of this condition. In fact, results with penicillin alone have been if anything slightly

better than with heparin added. Furthermore, it is the authors' impression that fewer embolic phenomena occur when heparin is omitted while the risk of hemorrhage is of course avoided and the treatment greatly simplified.

There are, however, two possible indications for the use of heparin in treating certain cases. First: in some instances in which large emboli have lodged in major vessels, it may be advisable to heparinize the patient in order to prevent retrograde thrombosis in the artery and thus to keep the collateral circulation open. Second: when extremely large doses of penicillin, say 5,000,000 to 10,000,000 units per 24 hours, are employed, thrombophlebitis at the site of intravenous infusion commonly occurs. Heparin may be useful in minimizing this complication of therapy. The authors have, however, successfully administered 10,000,000 units per day * by constant intravenous drip for as long as 16 consecutive days without employing anticoagulant therapy.

In summary, it is the authors' opinion that the use of heparin in treating bacterial endocarditis is contraindicated except under the specific circumstances mentioned above.

Part IV. Follow-Up Report on the 15 Patients Previously Reported

In an earlier paper [1] the authors reported on 15 patients who had apparently recovered from subacute bacterial endocarditis following penicillin therapy. The follow-up periods had varied from 22 months to one month at that time. These patients have now been observed over an additional 10-month period. There has been no evidence of recurrence of the infection in any of the 15 patients, nor has there been any change in their general health. None has died of other causes and none has developed cardiac failure. Repeated blood cultures have been sterile in all of the 15 patients. The follow-up periods in this group now range from 11 months to 32 months with an average of 18 months.

Combining the figures in the two groups reported by the authors we have the following results: of a total of 35 patients, 5 have died of all causes; the remaining 30 patients are all alive and apparently free from infection at the present time. The average period of follow-up for the entire group is 14 months.

Part V. Tentative Proposals for the Treatment of Subacute Bacterial Endocarditis with Penicillin

There is no doubt that penicillin is an agent of unprecedented value in the treatment of this disease. From the results herein reported it seems likely that the great majority of patients in *whom the offending organism is sensitive to penicillin* can be cured of the infection. The optimum regimen for accomplishing this end is not as yet clearly established, the principal

* This case will be reported in detail elsewhere by one of the authors (T. H. H.)

unanswered questions being: how much penicillin, by what route and for how long?

The answer to the first question, that is the daily dosage should probably be governed primarily by the sensitivity of the organism to penicillin. This is a biological measurement and as such is subject to many inherent inaccuracies. Furthermore, the translation of in vitro results into guides to therapy must necessarily be subject to question. Nevertheless, a rough approximation can be reached. As a working hypothesis it has been found advisable to maintain a serum level of penicillin at least four times as high as that amount required to inhibit the growth of the organism in vitro. This excess is perhaps necessary for penetration to the depths of the vegetations. On the other hand, there is some evidence that the discrepancy between in vitro measurements and levels of penicillin required in the blood may be explained by the different growth characteristics of organisms in broth and in the body.

In choosing the route by which penicillin is to be given, several possibilities must be considered. The oral administration of the drug may eventually become the method of choice. At present, however, there is little information pertaining to serum levels obtained by this method. Furthermore, results appear to vary considerably from patient to patient. The authors have had no experience with this route of administration but intend to investigate it in the future.

Although some patients unquestionably have responded favorably to penicillin given intramuscularly every two or three hours, it would appear desirable to administer the drug in a manner which assures a more uniform serum level. Therefore it is recommended that the constant intramuscular drip be used as the method of choice at present. Doses up to one or two million units per day can be given in this way without undue discomfort. For larger amounts it is advisable to employ the constant intravenous drip.

The most difficult problem in treating this disease is deciding how long to continue therapy. There are no recognized criteria for evaluating the status of the infection while therapy is in progress. One is forced to treat the patient for a given period, and then to discontinue at an arbitrary time. Further observation after stopping penicillin is the only means of judging the results. Fortunately the vast majority of relapses occur within a few days after cessation of therapy. In our experience the longest interval between treatment and relapse has been two weeks. Thus it is possible with a fair degree of certainty to tell within a short time whether or not a given course of therapy has been successful. It has therefore been our practice to start with a course of two or three weeks' duration, to which the majority of patients has responded favorably whenever the penicillin serum level has been adequate. When relapses have occurred, a second course of penicillin has been administered either using a higher daily dose or in rare instances employing the same amount per day over a more extended period of time. On the whole, better results have been obtained by increasing the daily dose

and thereby raising the level of penicillin in the blood, than by giving small amounts of the drug for protracted periods of time. In difficult cases, even though repeated relapses may occur, it cannot be too strongly emphasized that, if the infecting organism is sensitive to penicillin, eventual cure should be achieved barring complications such as cardiac failure or fatal embolic phenomena. There is no justification for abandoning hope of cure even though four or five courses of therapy have proved unsuccessful.

The foregoing recommendations have assumed access to a laboratory where measurements of the organism's sensitivity to penicillin and of penicillin serum levels can be obtained. Under circumstances where such facilities are not readily available, it is suggested that an initial course of 500,000 units per day for two or three weeks be tried. If blood cultures remain positive, or if relapse occurs following cessation of treatment, it is advised that the penicillin sensitivity of the infecting organism be determined at all costs. Otherwise, valuable time may be lost and large amounts of penicillin needlessly wasted in treatment which this information would immediately show to be inadequate or hopeless.

TABLE II

Correlation of Penicillin Serum Levels with 24 Hour Dose Administered by Constant Intramuscular Drip

Daily Dose (units)	Aver. serum level (u/c.c. of serum)	Range of values (u/c.c. of serum)	Number of Determinations
200,000	.07	.03 − .28	19
300,000	.09	.07 − .28	4
500,000	.2	.025− .8	113
1,000,000	.56	.5 − 6.4	42
2,000,000	1.6−2.24	.56 − 4.48	21
5,000,000	3.2	1.6 −12.8	16
10,000,000	6.66	6.4 −51.2*	17

Serum levels were determined according to the method described elsewhere.[4]
* This very high level occurred in a patient with transient azotemia.

The measurement of serum levels of penicillin is not as essential to rational therapy as is knowledge of the sensitivity of the organism. The serum level can be predicted with reasonable accuracy from the daily dose of penicillin. Table 2 shows the levels of penicillin obtained in the serum on various doses of penicillin administered by intramuscular drip. Levels obtained by constant intravenous drip have been entirely comparable with those obtained by the constant intramuscular route in our experience.

SUMMARY

Thirty-five cases of subacute bacterial endocarditis have been treated with penicillin. The group includes 15 new cases and a follow-up on 17 of the 20 patients previously reported.

Of the 35 patients, 30 are alive and apparently cured of the infection. The average period of follow-up has been 14 months.

Some patients required very large doses of penicillin, in one case 92,000,000 units in repeated courses, for termination of the infection.

The rôle of heparin as an adjuvant to therapy with penicillin is discussed and the opinion expressed that in most cases its use is inadvisable.

Tentative proposals are advanced for the future treatment of this disease, stressing the importance of giving large daily doses for periods of two or three weeks.

With persistent therapy, it should be possible to cure the disease in the great majority of cases in which the infecting organism is sensitive to penicillin.

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AMEBIASIS IN MILITARY OVERSEAS RETURNEES *

By Donald F. Marion, Major, M.C., F.A.C.P., and Frederick N. Sweetsir, Captain, M.C., A.U.S., *Coral Gables, Florida*

Introduction

There is no accurate estimate of the incidence of amebiasis in the United States. The results of independent and uncoördinated local surveys have failed to predict an acceptable national figure because of the failure in most instances to utilize accepted criteria for uniform and dependable studies. Despite the incredibly divergent estimates which have been published in recent years, general agreement has tentatively placed the incidence of carriers somewhere between Craig's 10 per cent [1] and Faust's 20 per cent [2] of the total population. Recently Brown, McHardy, and Spellberg [3] have reported 14.1 per cent incidence in a Louisiana survey of ambulatory patients, and have commented, "Amebiasis is a common disease in the South." Other surveys have suggested that it is only a little less common in the North and West as well.

Apprehension has been expressed concerning the possibility that soldiers returning from service abroad may appreciably enlarge the existing domestic reservoir of amebiasis. The well known ubiquity of functional and bacterial diarrheas in all troops has not prevented reports of such symptoms in our overseas soldiers from strengthening this impression. Recent evidences of such anxiety have included the suggestion that all overseas returnees should receive treatment with amebicidal drugs on suspicion alone and without regard for the demonstration of *E. histolytica* in individual cases. The opportunity for a better understanding of the actual situation has been afforded by the availability of a representative group of military returnees from the more important geographical areas, and the facilities and personnel required for a well controlled and standardized survey.

Clinical Material

This report deals with the first consecutive thousand unselected cases to enter this hospital directly from overseas in 1944. Approximately 40 per cent of the group were returned because of predominantly surgical or orthopedic conditions, while of the 60 per cent who were admitted on the medical service, only about one third were returned because of gastrointestinal diseases. Nearly all were young males, with an average age of 29.6 years. Duration of overseas service ranged from three to 40 months, with an average for all cases of 11.5 months. Residence prior to entry into the military service represented all of the 48 states.

* Received for publication June 28, 1945.
From the AAF Regional Hospital, Coral Gables, Fla.

Method

A minimum of three stool examinations was made in each case. Specimens were obtained routinely following mild saline purgation, and were usually collected on alternate days, beginning with the day after admission. All specimens were sent to the central laboratory soon after passage, and none was accepted after 11 a.m. to guard against appreciable drying or cooling before the stools reached the examiner. All samples were examined by technicians with adequate special training of six months or more, under the direction of an experienced parasitologist. Each specimen was subjected to three procedures: (1) direct fresh smears, with or without the addition of Lugol's solution, (2) iron-hematoxylin stained smears, and (3) zinc sulphate centrifugal flotation. All positive cases are represented by a fixed stained smear which is filed in the central laboratory.

Incidence

Chart 1 indicates the geographical areas in which the major portion of the overseas time was served. Many of these individuals served for shorter periods in one or more different locales, and nearly all passed through more than one geographical region en route to their ultimate destination. It is

Chart I

Geographical Area	Number	Positive Cases	Percentage
Temperate:			
England	66	10	15.2
North Pacific Alaska	7	1	14.2
Total	73	11	15.1
Subtropical:			
Mediterranean	249	46	18.4
Caribbean	71	8	11.2
Total	320	54	16.8
Tropical:			
Central and West Africa	34	4	11.8
South America	90	11	12.2
South Pacific	65	10	15.4
China, Burma, India	418	78	18.6
Total	607	103	17.0
Grand Total	1000	168	16.8

obvious that the total number of cases representing some of the areas is too small for the determination of a reasonably accurate incidence. For this reason the larger divisions; temperate, subtropical, and tropical have been included to reduce the margin of unavoidable error resulting from failure to discover *all* of the positive cases. Perhaps the most striking impression gained from these data is the relatively high incidence in those who served exclusively in temperate zones, although it is now well known that amebiasis is endemic in the British Isles as in all other countries.

Chart 2 is included because of the strong likelihood that many of the positive cases existed prior to enlistment in the Army, or at least prior to departure for overseas service. Careful surveys were obviously not possible at the time of induction, but it is not unreasonable to suppose that if such studies had been made the incidence would have approximated or exceeded the findings of Sapero and Johnson [4] who examined Naval recruits and found the incidence 14.7 per cent in the South and 7.8 per cent in the North. The small number representing the Mountain and Pacific Coast states pre-

CHART II]

Residence Prior to Military Service	Number	Positive Cases	Percentage
North East	307	49	15.9
North Central	265	43	16.3
South East	225	46	20.4
South Central	138	25	18.1
Mountain	37	3	8.1
Pacific Coast	28	2	7.1
Total	1000	168	16.8

North East: New England, N. Y., Pa., N. J., Del., Md., D. C.
North Central: Ohio, Mich., Ind., Ill., Wis., Minn., N. D., S. D., Nebr., Iowa.
South East: W. Va., Va., N. C., S. C., Ga., Fla., Ky., Tenn., Miss., Ala.
South Central: Kans., Mo., Ark., Okla., La., Tex.
Mountain: N. Mex., Ariz., Nev., Colo., Utah, Idaho, Wyo., Mont.
Pacific Coast: Wash., Ore., Calif.

cludes ready acceptance of the apparent lower incidence for this area. The fact that northern states are represented by more than half of the group suggests the need for an upward revision of previously accepted estimates therefrom.

The total incidence for the group, 16.8 per cent, does not represent a figure significantly higher than that of many reported estimates for domestic amebiasis. If this small sample is in any way indicative of what may be expected in subsequent returnees, there is little basis for apprehension regarding post-war increases in this disease. It is, of course, difficult to estimate the danger of the possible introduction of new strains of *E. histolytica* at this time, as Florio [5] suggests. With maintenance of high levels of sanitation and personal hygiene, however, it is unlikely that such eventuality will represent serious danger to the public health.

CLASSIFICATION

Although opinion differs regarding relative frequency of occurrence, three main types of amebiasis are recognized. There is little argument about the criteria for acute amebic dysentery, but little or no agreement has been reached in the establishment of a clear symptomatology for chronic amebic dysentery. The predilection of many clinicians for separation of the carrier-state into a symptomatic and an asymptomatic state leads to further

confusion in classification and much overlapping between the chronic dysentery group and the carrier group. Most of the discrepancy regarding relative incidence of the three types has been caused by the all inclusive and sometimes extremely vague symptoms attributed by many to the presence of *E. histolytica* in the bowel. Chart 3 reveals the type of infestation present on admission in the positive group of 168 cases. It is strikingly significant that 76.2 per cent are *totally* asymptomatic carriers despite the well known influence of a strange and often dangerous environment in the creation of a functional gastrointestinal disturbance. Quite certainly, a large number of

CHART III

Anaylsis of the 168 Positive Cases

	Acute	Chronic	Carrier State
Number of Cases	6	34	128
Percentage of Total Positive Cases	3.6%	20.2%	76.2%
Trophozoites only	3	13	32
Cysts only	1	16	76
Trophozoites and Cysts	2	5	20
Examined by Proctoscope	6	30	96
Ulceration Noted on Proctoscopy	5	6	3
Percentage With Demonstrable Ulceration	83.0%	20.0%	3.1

the 20.2 per cent classified as chronic amebic dysentery actually belong in the carrier group, and could be so classified were it not for the coexistence of a functional diarrhea or symptoms of irritable colon. Most of these became asymptomatic after appropriate treatment for amebiasis, but one must not overlook the salutary effect of returning home upon functional symptoms created primarily by overseas service.

Many in this group, as well as most of those in the acute amebic dysentery group, had received early and vigorous treatment with amebicidal drugs in overseas hospitals prior to their return. Without question this is the explanation of the very low incidence of both dysenteric amebiasis and the extraintestinal complications of amebiasis in returnees. Although occasional cases of amebic hepatitis and amebic hepatic abscess have been returned, the number has been small and there were none in this group of one thousand.

DISCUSSION

The epidemiological significance of the *E. histolytica* carrier depends to a great extent on the degree to which the organism can be considered essentially saprophytic or at least harmlessly parasitic, in the same manner as certain strains of *E. coli, E. nana,* and a host of other protozoan bowel inhabitants. Faust [6] has suggested that certain cases may demonstrate a minimal amount of superficial mucosal disease, but suggests further that there is very likely no such condition as a perfect balance between host tissue

and parasite. Many of the non-pathogenic protozoa, particularly certain of the flagellates, have been very suggestive causative agents in abdominal disturbances, including diarrhea states, where lowered intestinal mucosal resistance has been caused by one mechanism or another. In a similar manner the *E. histolytica* carrier-state may be converted to acute or chronic amebic dysentery. The rôle of bacillary dysentery in effecting this change has been suggested by Horster,[7] and the nutritional deficiencies developed by many soldiers stationed in remote areas could also be a major factor in such conversion. All of the positive cases have been treated intensively

CHART IV

Coexistent Protozoa	Acute	Chronic	Carrier State
E. coli	2	3	24
E. nana	1	7	30
Giardia lamblia	0	3	9
Dientameba fragilis	0	1	1
Trichomonas hominis	0	1	3
Chilomastix mesnili	0	1	2
Iodameba butschlii	0	0	1
Total cases demonstrating one or more coexistent parasites	3	8	42
Percentage infested with coexistent protozoan parasites	50.0%	23.4%	32.9%

with the simultaneous administration of carbarsone and one of the iodohydroxyquinolines, usually chiniofon or diodoquin.

It is of some interest to note the coexistence of other protozoan parasites in the *E. histolytica* positive group, as indicated in chart 4.

SUMMARY

1. In 1000 consecutive unselected military returnees from overseas service, *E. histolytica* was demonstrated in 168 or 16.8 per cent.

2. The highest incidence occurred in individuals who had served in tropical areas overseas, and in those who resided in Southern States prior to enlistment in the Army.

3. Of the positive cases, 76.2 per cent represented the asymptomatic carrier-state, 20.2 per cent chronic amebic dysentery, and 3.6 per cent acute amebic dysentery.

4. Prompt and intensive treatment of all proved and suspected cases in overseas hospitals explains the low incidence of dysenteric amebiasis and amebiasis complications.

5. The incidence herein reported is not significantly higher than that reported by many surveys conducted in the United States.

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TSUTSUGAMUSHI FEVER: AGGLUTINATION REACTIONS AND CLINICAL OBSERVATIONS IN 25 CASES *

By IRVING GREENFIELD, Captain, M.C., F.A.C.P.

RICKETTSIAL diseases have been known to man for over a thousand years.[1] With the advent of World War II, a large concentration of our armed forces has been on active duty in the regions of the globe where rickettsial diseases are endemic. One of these rickettsial diseases, epidemic or Old World typhus, has been the subject of concern in the past. As the result, considerable knowledge concerning it has been accumulated.[2]

Tsutsugamushi fever, one of the other rickettsial diseases, is an acute febrile disease transmitted to man by the bite of the larval stage [3] of the kedani mite. Clinically, it resembles the other rickettsial diseases. Information concerning this specific disease is comparatively scant. It was deemed of value, therefore, to publish this report in order to make as many observations as possible available for future studies.

Synonyms. The variety of descriptive terms employed to identify this particular rickettsial disease referred to the mite borne disease as it occurs in the endemic areas of southern Asia, and the islands of the Southwest Pacific. Thus, one finds that Japanese River fever, kedani fever, Japanese flood fever, tsutsugamushi fever, scrub typhus fever, Mossman's fever of North Queensland and pseudo-typhus of Sumatra have been used to indicate the same clinical disease.

Etiology. The etiological agent was described in 1920 by Hayashi.[4] Ogata [5] subsequently confirmed the observations which linked *R. tsutsugamushi* etiologically to Tsutsugamushi fever. *R. niponica, R. orientalis,* and *R. tsutsugamushi* were names used in different communications to indicate the agent etiologically responsible for this infection. Immunological studies on rabbits and monkeys were performed by Lewthwaite and Savoor [6] who established the fact that tsutsugamushi fever of Japan and scrub typhus of the Federated Malaya States were identical. Since these diseases were shown to be immunologically identical, it follows that they have identical etiological agents.

Reservoir. There is evidence to suggest that the disease is readily transmitted to white mice and other rodents. It is transmitted from these reservoirs to man by the bite of the larval form [3] of a mite *Trombecula acarina.*[7]

Epidemiology. The group of 25 cases reported in this communication occurred in a small coastal area of New Guinea in the foothills of the Owen-Stanley mountains where the annual rainfall is between 200–300 inches. The greater part of the rainfall occurs between May and August. Kunai

* Received for publication June 23, 1945.

grass, approximately three to four feet in height, is abundant. Dense jungle, mud, and a thick underbrush add to the conditions so favorable to the natural habitat of rodents and for the development of the mite. Infection occurred among troops who were assigned to work details which cleared areas of Kunai grass, and were either on maneuvers or on bivouac in the jungle. Since all of the cases occurred in military personnel, the age group was a young one. Three were in their late teens. Two were in the 30–40 year bracket. The remainder were in the 20–30 year group. One of the patients was a female who spent an afternoon on authorized recreation in an area where the Kunai grass had not been cut.

Incubation Period. We were unable to determine the date of inoculation. However, all of the patients were on duty in areas where conditions suitable for growth and development of larvae existed. Lippman and his co-workers [8] estimated that an incubation period of less than two weeks was common. The only known exposure in one of the patients reported in this communication was an assignment to a detail which cleared an area of kunai grass one week before his hospitalization. On admission he complained of malaise, aches and pains in his joints, and fever. He had a fully developed eschar on the perineum. The incubation period in this particular case was no more than four days. Another patient ran a low grade fever for a period of two weeks prior to admission. During this time he also had three chills. His course was hectic for five days during which his temperature fluctuated between 101° and 105° F. The titer of the Weil-Felix reaction, which on admission was negative in a dilution of 1:20, rose to positive in a dilution of 1:40 on the sixth hospital day when his temperature dropped sharply. Another patient complained of loss of appetite and malaise for four days prior to admission. During this period he had two chills. He, too, ran an extremely toxic course, with delirium, pulse irregularity, abdominal distention, and feeble heart tones. His systolic blood pressure, in mm. of mercury, dropped from 130 mm. to 90 mm., and the diastolic pressure dropped from 90 mm. to 50 mm. Neither of the latter patients had an eschar. Blood drawn from these patients on the day following the initial break in the fever demonstrated a rising titer of agglutination. The incubation period in these three cases varied from four days to two weeks. Prodromal symptoms which consisted of malaise, headache, chills, fever, loss of appetite and varying degrees of weakness together with multiple pains and aches were present in all of the patients for a period which varied from four days to two weeks prior to their admission to the hospital.

Symptoms. Most of the patients were admitted with a diagnosis of fever of undetermined origin and since blood smears which were taken routinely to rule out malaria were negative, we were able to obtain a clear and uncomplicated picture. The symptoms noted on admission are listed in the order of their frequency in chart 1. Headache, weakness, and fever were complained of by all. The headache varied in type and severity. It was described as aching, pounding, splitting or blinding. The weakness, as

described, varied from a slightly increased ease of fatigability to almost complete exhaustion. Backache and loss of appetite were next in the order of frequency. Of the group of 16 who complained of pains in the joints, two were admitted to the orthopedic service with a diagnosis of lumbosacral strain. The presence of an eschar suggested the diagnosis which was subsequently proved by a rising titer of agglutination. Two complained of a cough which was dry, hacking and non-productive. Neither had evidence on physical examination or on roentgenographic study to indicate parenchymal lung disease. Hyperesthesia, an uncommon complaint, was considerably troublesome in one patient with a most severe headache. Universal cutaneous hyperesthesia was so marked that the patient could not tolerate the weight of the bed sheets. One of the patients who complained of stiffness of the neck had sufficient nuchal rigidity to indicate a lumbar puncture. Examination of the spinal fluid revealed no abnormalities other than a slightly increased manometric pressure.

CHART I

Symptoms in Order of Frequency

Symptoms	Incidence
Headache	25
Loss of appetite	25
Fever	25
Malaise	20
Backache	20
Soreness of muscles	17
Soreness in joints	16
Chills	25
Frequency of urination	3
Stiffness of neck	3
Hyperesthesia	3
Cough	2
Fatigue	3

Physical Examination. The findings on physical examination lend themselves to division into two general groups: those which were present on admission, and those which developed during the course of the disease. The paucity of physical findings on admission was amazing. The patients were usually acutely ill, yet they presented very few positive features. Among the more typical findings were those present in the skin. The most characteristic of these was a small necrotic ulcer which may be present anywhere on the body. It occurred at the site of the mite bite, was usually 2–5 mm. in diameter, and had a black necrotic center which was surrounded by a red areola. It may also be present as a raised, indurated lesion with a yellowish apex. Removal of the skin at the apex of the lesion usually exposed the crater of the underlying ulcer. Characteristically, the eschar did not suppurate. It was painless and frequently remained unnoticed unless it was on an obviously exposed area. Eschars were present in 80 per cent of the cases herein reported. They were located on the perineum, axilla, the lower extremities, scalp, and breast. They were present in 72 per cent of Lippman's [8] cases and in 32 per cent of those reported by Ahlm and Lipshutz.[9]

Two of the patients were admitted with the rash in the early phases of its eruption. It consisted of a rose colored maculo-hemorrhagic lesion. The erythema which was deepest in the center of the macule faded out toward the periphery. The lesion measured 3–5 mm. in diameter, was discrete, did not fade on gentle pressure and showed no tendency toward coalescence. A hectic malar flush of the type seen in acute exanthematous diseases in children was present in four cases.

Lymphadenopathy was the next most common positive finding. Regional lymphadenopathy was present in all of the patients who had an eschar and in some who did not have them. One patient was admitted with a diagnosis of lymphadenitis, acute, non-suppurative, non-venereal of undetermined origin. Aside from the malaise, lassitude, slight headache, and elevated temperature, his only positive finding was two enlarged, tender, post-cervical glands which were about the size of an unshelled peanut. A rise in the agglutination titer established the diagnosis. Far more commonly, though, the regional lymph nodes draining the eschar were enlarged, tender and painful. The glands were discrete, firm, freely movable and tender. Universal lymphadenopathy was present in four patients. Multiple chains of enlarged glands were not uncommon. The spleen was found enlarged on admission in eight cases. It presented all of the characteristics of an acute infectious splenomegaly. Its size varied from one which was palpable at the costal margin to one palpable 1½ fingers'-breadth below the border of the last rib.

Next in the order of frequency were the ocular findings. Moderately severe conjunctivitis was present in 14 patients (56 per cent). Thirteen of the patients (52 per cent) complained of pain on performing extraocular movements and preferred not to use the ocular muscles because of the discomfort which resulted. Eight (32 per cent) had moderately severe photophobia. One patient had a small subconjunctival hemorrhage.

Two patients had a dry, hacking cough with a moderate pharyngitis. In both cases examination of the lung, clinically and roentgenographically failed to reveal any abnormality.

Clinical Course. By the seventh day of the disease, the rash had erupted in 88 per cent of the cases. It varied in intensity, usually made its appearance on the thorax first, and then spread to involve the abdomen, shoulders, neck and arms. One patient had a few lesions on his face. The eruptive phase once started required about 48 hours for its completion. The lesion lasted about four days and then faded. In several instances, residual light brown blotches of pigment remained at the site of the lesions for as long as eight days. There was no correlation between the severity of the clinical course and the intensity, phase of development, or duration of the rash.

Lymphadenopathy was present at some time during the course of the disease in all of the cases. The glands remained tender for three to five days. Splenomegaly was present on admission in eight cases and developed subsequently in three additional cases. One was associated with a peri-

splenitis. This patient complained of pain in the left lower chest which cut his breath short, was sticking in character, and was aggravated by deep breathing. No friction rub was audible. A bedside film revealed no abnormalities of the pleura or the lower lobe of the left lung. In the majority of cases, the spleen remained enlarged and slightly tender for three or four days and then returned to normal. Because of marked abdominal distention it was not possible to determine the duration of the splenomegaly in some of the acutely ill cases.

All of the patients ran a febrile course. There was no type of temperature curve which could have been considered characteristic. Some were remittent and were associated with daily chills recurring for two to five days. Others were maintained on an even plateau, between 104°–105° F., for several days. Very few ran a low grade fever. The average duration of fever was 11.3 days, the extremes being three and 20 days. Defervescence by crisis occurred in nine toxic cases. It occurred after five to seven days of a sustained type of fever. During this period the patients were acutely ill. In the remainder, the temperature fell by lysis. In this latter group were several severely toxic and acutely ill patients. In the recovery phase, the initial defervescence whether by crisis or by lysis was often followed by a secondary rise in the temperature, lasting from one to three days.

As a rule, the pulse rate remained slow and out of all proportions to the elevation of the temperature. A pulse rate of 80 or 90 a minute when the temperature was elevated to 103° or 104° F. was the rule. Early in the course of the disease, a dicrotic pulse was not uncommon. In the toxic cases the onset of myocardial involvement indicated by a rise in the pulse rate occurred between the fifth and seventh day. Gallop rhythm, ventricular premature contractions and an indeterminate type of arrhythmia were noted. A tic tac type of embryocardia with a sudden rise in the pulse rate above 120 beats per minute was present in three of the critically ill patients. The precordial impulse which on admission had been visible, palpable, forceful, and localized became diffuse. The cardiac dullness was widened to percussion. The heart tones were distant and indistinct. A soft, short, localized, apical systolic murmur was audible. Cyanosis of the lips and nail beds without evidence of pulmonary congestion was present. These findings were of short duration and subsided following defervescence.

Symptoms referable to the nervous system were interesting. Insomnia was the rule. Retroörbital and frontal headaches were present universally. They were severe and in several cases lasted throughout the duration of the pyrexia. In spite of the hyperpyrexia and in spite of the fact that they appeared acutely ill, most of the patients were pleasant and coöperative. Some were mildly euphoric for several days during which there were no complaints. However, after five or six days of persistent fever, sweats, and headaches, the euphoria gave way to apprehension. An attitude of complete satisfaction and coöperation was replaced by one of indifference

and negativism. Two patients resented being disturbed for therapy and nursing care. Muscular twichings were present in two cases. Neither showed evidence of impaired renal function or had nitrogen retention. Irritability and restlessness were evident. Four patients were extremely irritable and two were delirious for several days preceding the defervescence. Two patients developed a peripheral neuritis. One involved both peroneal nerves; the other involved the right brachial plexus. Both made a complete recovery after a prolonged period of hospitalization.

Pharyngitis developed during the course of the disease in 10 patients. All of them had a nonproductive cough. Four developed an intractable cough which was exhausting, kept them awake at night, and added to their discomfort. Bedside films revealed evidence of increased peribronchial and hilar markings. The findings were consistent with a roentgenographic diagnosis of bronchitis. One patient developed consolidation of the right base on the tenth day of the disease. A clinical diagnosis, which was confirmed roentgenographically, of pneumonia involving the right lower lobe was made. In addition, the right costophrenic sinus was obliterated. There was no pleural effusion. Though the pneumonitis was considered a complication of the disease, it was felt that the adhesive pleuritis was the residuum of pneumonia which had been contracted in childhood.

A moderate degree of dehydration was evident in many of the cases. The tongue was coated and dry. It resembled a strawberry tongue in that its edges and tip were acutely congested. Profuse perspiration was noted in three patients. Weight loss which ranged from 15 to 62 pounds occurred in every case. The outstanding feature of the disease was the profound prostration which was noted in all of the cases.

Abdominal distention was marked in three of the cases. It occurred between the fifth and seventh days of the disease and lasted four, five and six days respectively. In two cases it was so marked as to add to the pulmonary embarrassment already present. In one case it was severe enough to suggest a paralytic ileus. Constipation which responded to mild catharsis was the rule. None of the patients had diarrhea.

The course of the disease was such that the cases could easily be divided into three groups, mild, moderate, and severe. The mild and moderately ill patients presented no major problems and ran what might be regarded as an uneventful course. The severely ill patients ran an unpredictable course and with the onset of defervescence, a dramatic change occurred. Within the space of a few hours, a markedly toxic, severely distended, dyspneic, cyanotic, irrational, and often delirious patient awakened from sleep with a smile on his face, drenched with perspiration, and volunteered the information that he felt better. From that point, convalescence although prolonged because of profound weakness and exhaustion, was uninterrupted. The average duration of the hospital stay for the entire group was 41.7 days with extremes varying between 20 and 91 days.

Laboratory Data. There was no alteration in the red cell count or the hemoglobin. The white cell count did not differ markedly from that which was observed in the average patient admitted to the general medical service of any hospital in this area. A mild leukopenia of four to six thousand cells was the rule. Five patients had a white cell count below four thousand. With the onset of complications, one a reactivation of a quiescent pyelitis, another a complicating pneumonitis and three cases of bronchitis, a rise in the white cell count up to 12,000 with a polymorphonuclear leukocytosis was observed. With the exception of the patient who developed recurrent pyelitis, no pathological elements were found in the routine admission or subsequent urinalyses. The exception was a 22 year old soldier who gave a history of having had pyelitis in childhood. He was very vague as to the circumstances surrounding his initial infection but stated that on two or three occasions, following an upper respiratory infection, urinalyses revealed the presence of pus cells. The admission urine specimen contained red cells, clumps of white cells, granular casts, and albumin. A leukocytosis of 9,300 cells with 80 per cent polymorphonuclear leukocytes was present. Blood chemistry revealed normal urea, total protein, and albumin-globulin ratio. A rising titer of the Weil-Felix agglutination reaction supported the diagnosis of typhus fever.

The observations made in this study are in complete accord with those who stated [9, 10] that there was no correlation between the height of the agglutination titer or the rapidity with which it rose and the clinical course. Neither could any relationship between the presence or absence of the eschar and the Weil-Felix reaction be established. Some observations in regard to the Weil-Felix reaction merit attention. In order to facilitate matters the reader is referred to chart 2. Columns 1, 2, and 3 are self-explanatory. In column 4 is recorded the day of the disease on which the OXK titer of agglutination reached its peak. Column 5 records the highest dilution of the agglutination titer. Column 6 shows the day on which the peak of the agglutination titer was reached in relation to the day on which defervescence started. The last column records the duration of the positive reaction.

One must regard the Weil-Felix reaction in the same light as one does the Wassermann test. Typhus fever, therefore, cannot be excluded from the differential diagnosis because of a persistently negative agglutination reaction.[11] The reaction is of value when it is positive in dilutions of 1 : 160 or when one can demonstrate a rising titer of OXK agglutinins in specimens of blood taken at intervals of several days. The former group is of diagnostic significance, whereas the latter may be accepted as presumptive evidence in favor of the diagnosis. Positive reactions were obtained in 21 cases (84 per cent). The dilutions were sufficiently high in eight of the cases to be considered diagnostic. In the interval between the fourth and the thirteenth days of the illness a rise in agglutination titer was demonstrated in the remaining 13 patients. The Weil-Felix reaction remained negative in four cases.

Agglutinins for OXK in a dilution of one to 40 (1:40) or over were present in the first specimen of blood examined in four of the cases. Two of these showed a subsequent rise in the titer. One, taken on the sixth day of hospitalization or on the day on which defervescence started, contained OXK agglutinins in a dilution of 1:160. In the other case the specimen of blood was taken on the thirteenth day of the disease or when viewed from the temperature chart on the day following the start of the defervescence. OXK agglutinins were present in a dilution of 1:640. The Weil-Felix test was not repeated in the remaining two cases.

CHART II

Case No.	Day of dis. 1st W-F Reaction was taken	Result	Day of dis. OXK titer reached peak	Dil. in which OXK was positive	Rel. bet. height of pos. titer and deferv.	Follow-up WF Reaction
1	2	Neg.	5	1:80	+1 da.	N 8th day
2	3	Neg.	7	1:40	+1 da.	N 2nd day
3	12	Neg.		Neg.	+5 da.	
4	5	Neg.	11	1:80	+2 da.	N 14th day
5	3	1:40	6	1:160	0	N 7th day
6	2	Neg.	7	1:40	−1 da.	N 8th day
7	8	Neg.		Neg.	+3 da.	
8	7	Neg.		Neg.	−3 da.	
9	6	Neg.	15	1:320	0	
10	9	1:80	9	1:80	+1 da.	N 2nd day
11	3	Neg.	10	1:1280	+1 da.	P 14th day
12	6	1:40	13	1:640	+1 da.	P 10th day
13	8	1:640	8	1:640	+1 da.	
14	1	Neg.	11	1:160	+1 da.	
15	7	1:80	7	1:80	−5	N 14th day
16	4	1:40	4	1:40	−3	N 8th day
17	7	1:160	7	1:160	+1	
18	2	Neg.	13	1:160	+1	N 6th day
19	10	Neg.	17	1:320	0	P 3rd day
20	4	Neg.		Neg.	−6	
21	3	Neg.	9	1:80	+1	N 2nd day
22	1	Neg.	12	1:40	0	N 3rd day
23	5	Neg.	8	1:80	0	N 3rd day
24	2	Neg.	10	1:40	+1	N 4th day
25	2	Neg.	7	1:80	+1	N 4th day

A rise in the agglutinin titer was demonstrated in 17 cases. Of these, eight reached dilutions of over 1:160. The remaining nine cases demonstrated a rise in titer in the lower dilutions (i.e., 1:40 or 1:80). Engrafting the date on which the agglutination titer reached its peak on the temperature chart, it was observed that a close relationship existed between that day and the day on which defervescence started. Since the duration of the pyrexia is variable, it is not possible to predict the date on which defervescence will start. However, by watching the temperature curve carefully, it may be possible to select the time at which it would be reasonable to expect that the Weil-Felix reaction would be positive in the higher dilutions. In this small series of cases that period of time which elapsed between the day preceding and the day following defervescence appeared to be optimal. The

series is too small to permit any definite conclusions to be drawn, but the observation was sufficiently striking to warrant further study. It is known that the reaction becomes positive some time during the second week of the disease. The observation cited simply narrows this period down to the time of defervescence. Those reactions which were positive in the high dilutions 1:320 or over, remained positive for upward of a week. Those which were positive in the dilutions below 1:160 had a tendency to fall within a period of two to four days after it had reached its peak. There were four cases in which the agglutination reaction remained negative. The first patient had an eschar on her right breast, enlarged, tender glands in the right axilla, ran a low grade type of fever, and developed a rash on the sixth day of hospitalization. Defervescence occurred on the seventh day. The blood for the Weil-Felix reaction was not drawn until the twelfth day or five days after defervescence had occurred. The second was admitted with photophobia, a rash on his chest, and an eschar on the left tibia situated approximately two inches above the internal malleolus. Defervescence started on the sixth day when the temperature dropped from 104° to 101° F. It then took two days for the temperature to reach the base line. Blood for the Weil-Felix reaction was drawn on the ninth hospital day or three days after the initial break in the fever. Case three had an eschar on the dorsum of the right foot, a universal lymphadenopathy, and a typical rash. He was extremely toxic during the last four days of his fever which was of the remittent type and lasted 10 days with daily fluctuations ranging between 102° and 105° F. Blood drawn on the sixth day of the disease or three days before the start of defervescence contained no agglutinins in a dilution of 1:20. No subsequent examinations were made. The fourth had an eschar on the scrotum, axillary and inguinal lymphadenopathy, a typical rash, and a remittent type of fever for 11 days. Defervescence occurred on the twelfth day of the disease. He ran a moderately severe course. Specimens of blood drawn the fifth and eighth days of the disease contained no agglutinins. Additional specimens were not submitted. In the light of the observations reported in this communication it is suggested that the agglutination reaction might have shown a rising titer had the specimens been taken at the time of defervescence.

Pathology. None of the cases studied in this series died. A discussion of the pathology of typhus fever is, therefore, beyond the scope of this communication. However, the reader is referred to an excellent article by Corbett [12] who found that the primary lesion was a diffuse vasculitis and perivasculitis. Some of his cases exhibited a tendency toward thrombus formation.

Therapy. In the absence of any specific type of therapy, the importance of complete rest and adequate nursing care cannot be overestimated. Since the treatment is purely symptomatic, the desire to keep the patient comfortable will often constitute a challenge to the therapeutic skill and resource-

fulness of the physician. Its objective should be to allay fear and apprehension and to maintain adequate nutrition. Barbiturates, hypnotics, and narcotics were often necessary to control the headache, insomnia, and restlessness. Acetylsalicylic acid in small repeated doses was often of value in relieving the headache. Frequent sponges are indicated when the fever reaches its peak. The use of an ice cap will occasionally be comforting. In view of the sustained hyperpyrexia supplementary vitamin therapy is of considerable importance. To combat dehydration, the fluid intake was maintained at between three and four liters a day. However, due caution was exercised to avoid overloading an already injured cardiovascular system. Small amounts, one to two units, of plasma were given daily in the severely toxic cases. Whole blood transfusions and a high protein diet when oral feeding is possible seem to be of value. Fruit juices were given freely except in those cases where abdominal distention was a disturbing factor. A variety of enemata, Murphy and Harris drips, rectal tube, pitressin, etc., were employed at various times to alleviate the abdominal distention. Marked prostration often makes colonic irrigation a hazardous procedure, so that one hesitates to use it. Oxygen was given empirically for the relief of dyspnea without demonstrable effect. However, five patients who received oxygen noticed that the headache was relieved. The use of cardiac depressants should be avoided. Cardiac, vascular, and pulmonary complications should be treated promptly as they arise. From the above it becomes evident that standardization of the treatment is not possible.

Summary

Twenty-five cases of scrub typhus fever observed in an area in the Southwest Pacific were studied. The observations reported in this communication were made from a careful study of the clinical course. The symptoms noted were those reported by the patients. The observations in regard to the physical findings were those which were noted in the record. The behavior of the Weil-Felix reaction was a matter of particular interest. Though the series is too small to permit of any definite conclusions, it suggests that a time might be selected in terms of one or two days when the peak of the agglutination titer might be predictable. The importance of this observation, if borne out by future study, cannot be overestimated in view of the fact that the laboratory facilities in military installations are often taxed to the limit of their capacity. The fleeting character of the positive agglutination reaction in the low titers may offer an explanation for the high percentage of negative reactions reported in some communications. It may also account for the four persistently negative reactions observed in this series.

Agglutination tests were made at the Fifth Medical Laboratory.

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ASIATIC RELAPSING FEVER; REPORT OF 134 CASES TREATED WITH MAPHARSEN *

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THIS report comprises 134 cases of relapsing fever of the Asiatic type. Relapsing fever is a spirochetal infection characterized by one or more attacks of fever beginning and ending abruptly and separated by an afebrile period of varying duration.

The disease is prevalent in many parts of the world and assumes the form of a virulent epidemic in famine stricken, debilitated populations. The causative organism is a spirochete of the genus *Spirochaeta* (*Borrelia*) and transmission is by infected lice or ticks. The spirochetes of relapsing fever have been separated by agglutination and other reactions into two groups—*S. recurrentis* (louse-borne), and *S. duttoni* (tick-borne).[1] There has been, in the past, a tendency to subdivide these two groups into various strains on a serological basis, but it is now generally held that differences in the organism are so slight that this is impracticable and sub-division is unnecessary.[2]

The spirochetes enter the body through abraded skin by contamination with crushed material from infected lice. Apparently, the bite of the louse alone does not transmit the spirochete. Though no special studies were made positively to identify the species of spirochete found in the cases presented, the evidence pointed to the louse-borne *S. recurrentis*. Almost every patient had stigmata of recent lice infestation. Information received from the camp in China from which they came was that a large percentage of their population was heavily infested with lice. Clinically, the marked tendency to collapse following a crisis is characteristic of the louse-borne type of relapsing fever. Moreover, no ticks were found on the patients and none gave a history of being bitten by ticks.

Material. The conditions surrounding these cases are important. All were admitted between December, 1943 and August, 1944, the majority being seen in May, June, and July, 1944. All were Chinese soldiers and all were treated in a U. S. Army Station Hospital situated in a remote section of Assam, India.

The Chinese were recruits who, fresh from coolie life in China, were flown over the Himalaya "Hump" into Assam. The majority had been in India less than one week before developing relapsing fever and a considerable number were ill at the time of making the flight. Delousing was done in both the Chinese and Indian camps. As the incubation period of relapsing fever is about seven to 12 days, it is probable that most of our cases contracted the disease in China.

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The air route over the Himalayas is one of the most hazardous in the world and is made at altitudes in the neighborhood of 20,000 feet. At such heights, these men were exposed to sub-zero temperatures and oxygen-poor atmosphere. There is no question but that the flight, under these circumstances, played a considerable part in lowering the general resistance of the individual. The Indian camp was located some distance from the hospital, and cases were transported by U. S. Army ambulance. Because of the distance to be traveled and because these troops arrived from China in large numbers, admission of Chinese to the hospital was usually in groups of 20 to 30. Inasmuch as supplies, personnel, and equipment were scarce during the time they were seen, it was impossible to make a detailed study of each case.

As a group, these patients were in exceedingly poor condition. Almost without exception, there were signs of malnutrition and multiple vitamin deficiencies. Many had frank beriberi, a large number had pellagra, and a few had scurvy. Almost 100 per cent of the stools examined contained ova, usually hookworm or *Ascaris lumbricoides*. Though blood counts were by no means routine, enough were done to give a fair index of the group. A hypochromic anemia was the rule, and in no instance was the erythrocyte count within normal limits. Many patients gave histories of typhus fever and repeated attacks of malaria in the past.

The Chinese soldier is in many ways an almost ideal patient, for he is fearless, willing and obedient within the limits of his understanding. However, the average Chinese soldier, particularly the recruit, has no conception of illness comparable to that of the American. Bed rest is almost impossible to enforce. Most of our patients would remain in bed only at the height of their fever or during a particularly severe chill. At other times, they would wander about the ward and frequently take possession of another bed. This led to confusion in identity and mistakes in medication. This was corrected by marking each patient's forehead with his chart number. These, and other similar factors, are of considerable importance in treating a large number of patients of foreign tongues and ways.

Histories were obtained through interpreters and at best, contained only the essential facts. No attempt was made to obtain more than a sketchy past history. In many instances, it was discovered that two interpreters gave entirely different histories on the same patient. This may be partly explained by the serious condition of the patients, but in general, the histories were unreliable. This was of particular importance when treatment was considered, as the duration of the febrile attack in relapsing fever is one of the determining factors in the institution of specific therapy. A few patients who succumbed, probably died because of inaccurate timing of treatment. This disturbing factor was partly overcome by the medical officers and nurses learning sufficient spoken Chinese to obtain a more reliable history.

Upon admission to the hospital, all patients were given a shower bath, and a search was made for lice. Only a very few were found to be harboring lice or nits.

Immediately on being put to bed, thick and thin blood smears were taken. These were stained with Giemsa stain and examined under oil immersion. A few fresh, wet preparations were made on the early cases, but as the volume increased, it became impracticable to use this method. Smears were repeated at frequent intervals until reported positive or until relapsing fever had been ruled out. Spirochetes were, in most cases, found on the first smear and were usually plentiful. Many smears showed tremendous numbers of organisms in each field, most often occurring in clumps of 10 or more. The number of spirochetes found on blood smears served as a rough guide to the severity of the infection. However, some of the critically ill patients showed only a few spirochetes and, rarely, a patient would show large numbers of the organisms with only mild clinical findings. All positive smears were checked by trained workers. Only those cases with *S. recurrentis* found in the blood smear are included in this series.

TABLE I

Clinical Summary of 134 Cases

Symptoms on Admission	No. of Cases
Fever	119
Muscular aching	116
Cough	85
Chills	64
Weakness	54
Constipation	51
Diarrhea	41
Dizziness	38
Physical Findings	**No. of Cases**
Transient râles	70
Splenomegaly	59
Muscle tenderness	52
Hepatomegaly	22
Jaundice	15
Conjunctivitis	11
Rash	7
Deafness	6

Clinical. (A summary of the clinical findings is seen in table 1.) On admission, the patients usually presented one of two striking clinical pictures. The more common was that of the febrile attack. The complaints were dizziness, fever, cough, headache and muscular pains. The temperature was of the sustained type, usually above 104° F., with the pulse rapid and full. Dehydration was marked with dry, hot skin and flushed, anxious facies. The conjunctivae were frequently injected. Wheezing râles and rhonchi with rapid, shallow respirations were common findings. The spleen and, less often, the liver were apt to be enlarged and tender. Tenderness in the calf muscles was a characteristic finding. This stage was abruptly terminated a few hours after the administration of an arsenical. However, there were many cases on whom treatment was withheld and the attack was allowed to run its course. It was found that the initial attack lasted from five to 15 days, whereas subsequent attacks were of much shorter duration,

rarely lasting longer than five days. The febrile attack in both instances ended in an abrupt crisis.

The second type of patient was that admitted in profound circulatory collapse following the crisis. Practically all of these men were in a critical condition and required immediate supportive treatment. The main complaints were thirst and marked weakness, particularly in the legs. The skin was cold and clammy in spite of evident dehydration. An ashen pallor was present. Apathy was marked. The temperature was usually below normal and the pulse was rapid and thready. Diarrhea was common in this stage. Splenomegaly was almost invariably present.

The length of the circulatory collapse varied considerably with individual cases, but in general, it rarely existed longer than 12 hours. In that time, the patient either recovered or succumbed.

Diagnosis. The clinical diagnosis of relapsing fever in a tropical zone is difficult. It must be differentiated from malaria, typhus, rat-bite fever, dengue, pappataci fever, and a host of other acute febrile conditions.

The frequency of respiratory symptoms and signs, notably those of bronchitis, is a clue to relapsing fever. The pulse is usually more rapid than in most tropical fevers. Weakness and prostration are pronounced and, coupled with pain and tenderness in the calves of the legs, are suggestive of relapsing fever. A polymorphonuclear leukocytosis is often, though not invariably, present.

The only certain means of diagnosis is through the detection of the organism in the blood smear. In this series, spirochetes were found in all stages of the disease but, as would be expected, were far more numerous during the febrile attack.

Treatment. Uncomplicated relapsing fever usually responds dramatically to intravenous arsenicals. Only one or two injections are required to effect a cure. In the past, epidemics have been reported in which salvarsan and neoarsphenamine were used with satisfactory results.[3]

In evaluating results from various drugs, the condition of the patients must be taken into account. The economic status of the patient plays a large rôle in the severity of the disease as the mortality rate in epidemics varies inversely with the nutritional state. As stated above, nearly every patient in the group from which these cases were taken was suffering from malnutrition and helminthiasis, and was therefore, in poor general physical condition. However, there were gradations in the severity of the reaction to relapsing fever and, for the purpose of tabulation, cases were classified as "good," "fair," or "poor," according to the estimated condition of each on admission (table 2). Those cases listed as in "good" condition were those who were in a remission and had few or no complaints or physical findings. Those listed as "fair" had only mild complaints and did not appear acutely ill. The majority of these patients were either in the early stages of the febrile attack or recovering from the crisis. Those admitted

TABLE II

Summary of Treatment and Results

Case Number	Condition on Admission	Marpharsen			Number of Days from Admission to Defervescence	Outcome	Number of Days from Admission to Death	Remarks
		Number of Injections	Dosage in Grams	Interval in Days Between Injections				
1	Fair	1	0.06		14	R*		Toxic reaction to mapharsen
2	Fair	1	0.06		12	R		Toxic reaction to mapharsen
3	Poor	1	0.06			D†	2	Died in circulatory collapse
4	Fair	1	0.06		2	R		Toxic reaction to mapharsen—parotitis
5	Poor	2	0.06 0.06	5	6	R		Recurrence—toxic reaction
6	Poor	2	0.06 0.06	2	4	R		Recurrence—toxic reaction
7	Fair	2	0.06 0.06	12	15	R		Recurrence—toxic reaction—parotitis
8	Poor	2	0.06 0.06	10	12	R		Toxic reaction to mapharsen—recurrence
9	Poor	2	0.06 0.06	5	6	R		Toxic reaction to mapharsen—recurrence
10	Poor	2	0.06 0.06	5	7	R		Toxic reaction to mapharsen—recurrence
11	Poor	2	0.06 0.06	7	8	R		Toxic reaction to mapharsen—recurrence
12	Poor	1	0.04			D	2	Died in circulatory collapse
13	Fair	1	0.04			D	2	Died from severe epistaxis
14	Poor	1	0.06		2	R		Toxic reaction to mapharsen
15	Poor	1	0.04			D	4	Died in circulatory collapse, hemorrhage from bowel
16	Poor	1	0.04			D	1	Died in coma
17	Good	1	0.06		2	R		Toxic reaction to mapharsen
18	Fair	1	0.04		2	R		Conjunctivitis
19	Poor	1	0.04		2	R		Conjunctivitis
20	Poor	2	0.04 0.04	3		D	7	Died in coma with hepatitis, rash
21	Good	1	0.04		2	R		Prompt recovery
22	Poor	1	0.04		2	R		Prompt recovery
23	Poor	1	0.04		3	R		Prompt recovery
24	Poor	1	0.04		20	R		Severe epistaxis—parotitis
25	Poor	1	0.04		2	R		Conjunctivitis—rash
26	Good	1	0.04		2	R		Prompt recovery
27	Poor	1	0.04		22	R		Hepatitis
28	Poor	1	0.04		2	R		Rash
29	Poor	1	0.04		3	R		Prompt recovery
30	Poor	1	0.04		14	R		Hepatitis—rash
31	Poor	1	0.04		2	R		Prompt recovery
32	Poor	1	0.04		3	R		Prompt recovery
33	Poor	1	0.04		2	R		Prompt recovery
34	Poor	1	0.04		2	R		Prompt recovery
35	Poor	1	0.04		7	R		Mild epistaxis, prompt recovery
36	Poor	1	0.04		3	R		Orchitis—prompt recovery
37	Fair	1	0.04		3	R		Prompt recovery
38	Poor	1	0.04			D	1	Died in circulatory collapse
39	Good	1	0.04			D	1	Died of convulsions and hyperpyrexia
40	Poor	1	0.04		14	R		Mild epistaxis, prompt recovery
41	Poor	1	0.04		2	R		Prompt recovery

* Recovered.
† Died.

TABLE II—*Continued*

Case Number	Condition on Admission	Marpharsen			Number of Days from Admission to Defervescence	Outcome	Number of Days from Admission to Death	Remarks
		Number of Injections	Dosage in Grams	Interval in Days Between Injections				
42	Fair	1	0.04		2	R		Prompt recovery
43	Poor	1	0.04		2	R		Prompt recovery
44	Poor	2	0.04 0.04	5	6	R		Recurrence, prompt recovery
45	Poor	2	0.04 0.04	5	7	R		Recurrence—mild epistaxis
46	Poor	1	0.04		10	R		Prompt recovery
47	Poor	1	0.04		15	R		Hepatitis—conjunctivitis
48	Poor	1	0.04		6	R		Rash—prompt recovery
49	Poor	2	0.02 0.04	3		D	6	Recurrent case, died with circulatory collapse
50	Poor	2	0.04 0.04	4	7	R		Recurrence—prompt recovery
51	Poor	2	0.04 0.04	3	12	R		Recurrence—hemoptysis, bowel hemorrhage
52	Poor	2	0.04 0.04	3	4	R		Recurrence—conjunctivitis
53	Poor	1	0.04			D		Died in coma
54	Fair	2	0.04 0.04	2	5	R		Recurrent case—conjunctivitis
55	Poor	1	0.04			D	1	Died of convulsions and hyperpyrexia
56	Poor	1	0.04			D	2	Died of bowel hemorrhage—hepatitis
57	Good	2	0.04 0.04	5	6	R		Recurrent case
58	Poor	2	0.04 0.04	3	4	R		Recurrent—rash
59	Poor	2	0.04 0.04	4	16	R		Recurrence—hepatitis, conjunctivitis
60	Poor	2	0.04 0.04	5	6	R		Recurrent case
61	Poor	2	0.04 0.04	4	5	R		Recurrent case
62	Poor	1	0.04			D	2	Died of circulatory collapse
63	Fair	2	0.04 0.04	3	4	R		Prompt recovery
64	Poor	2	0.04 0.04	3	5	R		Parotitis—conjunctivitis
65	Poor	2	0.04 0.04	4	5	R		Conjunctivitis—prompt recovery
66	Poor	2	0.04 0.04	3	4	R		Prompt recovery
67	Poor	2	0.04 0.04	3	4	R		Orchitis, prompt recovery
68	Poor	2	0.04 0.04	3	6	R		Parotitis
69	Fair	2	0.04 0.04	3	25	R		Mild epistaxis
70	Good	2	0.04 0.04	3	2	R		Hepatitis
71	Good	2	0.04 0.04	3	4	R		Hepatitis
72	Good	2	0.04 0.04	3	8	R		Prompt recovery
73	Fair	2	0.04 0.04	3	42	R		Hepatitis, hematuria, bowel hemorrhage

TABLE II—*Continued*

Case Number	Condition on Admission	Marpharsen			Number of Days from Admission to Defervescence	Outcome	Number of Days from Admission to Death	Remarks
		Number of Injections	Dosage in Grams	Interval in Days Between Injections				
74	Poor	2	0.04 0.04	3	2	R		Prompt recovery
75	Poor	2	0.04 0.04	3	4	R		Prompt recovery
76	Poor	2	0.04 0.04	3	2	R		Prompt recovery
77	Poor	2	0.04 0.04	4	2	R		Prompt recovery
78	Poor	2	0.04 0.04	3	3	R		Prompt recovery
79	Poor	2	0.04 0.04	5	14	R		Hemoptysis
80	Poor	2	0.04 0.04	3	2	R		Prompt recovery
81	Poor	2	0.04 0.04	3	2	R		Prompt recovery
82	Poor	2	0.04 0.04	3	2	R		Prompt recovery
83	Poor	2	0.04 0.04	3	2	R		Prompt recovery
84	Poor	3	0.04 0.04 0.04	3 and 10	21	R		Recurrent case, parotitis
85	Poor	2	0.04 0.04	3	4	R		Prompt recovery
86	Poor	2	0.04 0.04	3	2	R		Prompt recovery
87	Poor	2	0.04 0.04	3	2	R		Prompt recovery
88	Poor	2	0.04 0.04	3	2	R		Prompt recovery
89	Fair	2	0.04 0.04	3	*			*Afebrile on admission
90	Poor	2	0.04 0.04	3	1	R		Prompt recovery
91	Poor	2	0.04 0.04	3	6	R		Prompt recovery
92	Fair	2	0.04 0.04	3	*	R		*Afebrile on admission
93	Fair	2	0.04 0.04	3	*	R		*Afebrile on admission
94	Poor	1	0.02			D	1	Died in circulatory collapse—small hemorrhage from bowel
95	Poor	2	0.04 0.04	3	4	R		Prompt recovery
96	Poor	2	0.04 0.04	3	1	R		Prompt recovery
97	Poor	2	0.04 0.04	3	5	R		Prompt recovery
98	Poor	2	0.04 0.04	4	5	R		Prompt recovery
99	Poor	2	0.04 0.04	3	3	R		Prompt recovery
100	Fair	2	0.04 0.04	3	2	R		Prompt recovery

TABLE II—*Continued*

Case Number	Condition on Admission	Marpharsen			Number of Days from Admission to Defervescence	Outcome	Number of Days from Admission to Death	Remarks
		Number of Injections	Dosage in Grams	Interval in Days Between Injections				
101	Poor	2	0.04 0.04	3	5	R		Conjunctivitis—prompt recovery
102	Poor	2	0.04 0.04	3		D	5	Died of secondary parotitis—small hemorrhage from bowel
103	Poor	2	0.04 0.04	5	3	R		Prompt recovery
104	Poor	2	0.04 0.04	4	2	R		Prompt recovery
105	Poor	2	0.04 0.04	3	2	R		Prompt recovery
106	Poor	2	0.04 0.04	3	5	R		Myelitis
107	Poor	2	0.04 0.04	3	2	R		Prompt recovery
108	Fair	2	0.04 0.04	3	2	R		Prompt recovery
109	Poor	2	0.04 0.04	3	4	R		Hepatitis
110	Poor	2	0.04 0.04	5	2	R		Prompt recovery
111	Poor	2	0.04 0.04	3	2	R		Prompt recovery
112	Poor	2	0.04 0.04	3	6	R		Hepatitis
113	Poor	2	0.04 0.04	3	6	R		Prompt recovery
114	Poor	2	0.04 0.04	3	7	R		Prompt recovery
115	Poor	2	0.04 0.04	3	12	R		Hemoptysis
116	Poor	2	0.04 0.04	3	9	R		Hepatitis, parotitis
117	Poor	2	0.04 0.04	3	5	R		Prompt recovery
118	Poor	2	0.04 0.04	3	7	R		Prompt recovery
119	Fair	2	0.04 0.04	3	1	R		Prompt recovery
120	Fair	2	0.04 0.04	3	2	R		Prompt recovery
121	Poor	2	0.04 0.04	3	2	R		Prompt recovery
122	Poor	2	0.04 0.04	3	3	R		Prompt recovery
123	Poor	2	0.04 0.04	3	4	R		Prompt recovery
124	Good	2	0.04 0.04	3	*	R		*Afebrile on admission
125	Fair	2	0.04 0.04	3	2	R		Prompt recovery
126	Poor	2	0.04 0.04	3	5	R		Hepatitis
127	Poor	2	0.04 0.04	3	5	R		Hepatitis

TABLE II—*Continued*

Case Number	Condition on Admission	Marpharsen			Number of Days from Admission to Defervescence	Outcome	Number of Days from Admission to Death	Remarks
		Number of Injections	Dosage in Grams	Interval in Days Between Injections				
128	Poor	2	0.04 0.04	3	2	R		Prompt recovery
129	Poor	2	0.04 0.04	3	5	R		Myelitis
130	Poor	2	0.04 0.04	3	1	R		Prompt recovery
131	Poor	2	0.04 0.04	3	6	R		Conjunctivitis
132	Poor	2	0.04 0.04	3	26	R		Hepatitis
133	Poor	2	0.04 0.04	3	5	R		Prompt recovery
134	Poor	2	0.04 0.04	3	2	R		Prompt recovery

acutely ill, at the height of the febrile attack or during the stage of collapse, were listed as "poor."

Mapharsen (Meta-amino-para-hydroxy-phenylarsine-oxide-hydrochloride) was chosen in treating these cases because of its availability, its known low toxicity, and because of its ease of administration. So far as could be determined, no cases have been reported in which mapharsen was used in the treatment of relapsing fever.

At the outset of the epidemic, all cases received a single injection of 0.06 gram, but because of toxic reactions, this amount was reduced to 0.04 gram. Although one injection of 0.04 gram was often sufficient to effect a cure, the number of recurrences of the disease soon led to the routine use of two injections each of 0.04 gram, given three to five days apart.

In table 2 it is shown that frequently a second injection of mapharsen was given even though defervescence had already occurred. This was done to prevent recurrence. For example, case 90 was admitted with a history of fever, generalized aching and weakness of two days' duration. *S. recurrentis* were found on the first blood smear and, on the day of admission, the first dose of mapharsen was given. The following day the patient was up and about the ward area, afebrile and with no complaints other than weakness. In spite of an apparent cure at this time, a second injection of mapharsen was given on the fourth hospital day. He was discharged as cured on the twelfth hospital day. Nineteen cases (13 per cent) had a recurrence after two injections. The average recurrence occurred on the fifth day, but some were observed as soon as two, and as late as 12 days after the initial injection. The recurrence was in every way similar to the original

attack. However, spirochetes were rarely found on smears taken during a recurrence.

Spontaneous recovery in relapsing fever is known to occur but none was seen by us. Several patients were admitted with no complaints but with a history of a febrile episode just prior to admission. Four of these (cases 89, 92, 93 and 124) had smears positive for *S. recurrentis* on admission. Undoubtedly these patients were in a remission. Mapharsen was given and no further evidences of relapsing fever developed in any case. Other afebrile patients with suggestive histories failed to show spirochetes as long as they were afebrile. Most of these developed attacks within a few days and *S. recurrentis* were then found (cases 69, 70, 71 and 126). In each case mapharsen was given on the first day of fever and resulted in a prompt cure.

In about four hours following the initial injection, most patients developed increased pyrexia of 1 to 2° F. This was often accompanied by a chill and marked generalized aching. This phenomenon was interpreted as representing a reaction induced by the destruction of large numbers of spirochetes with the liberation of toxins and foreign protein. The pyrexia continued for several hours and generally terminated in an abrupt crisis. This was followed by a subnormal temperature and varying degrees of circulatory collapse. In an effort to minimize this reaction a few patients were given 0.04 gram of mapharsen dissolved in 1,000 cubic centimeters of physiologic saline. This was discontinued when results were found to be the same as when the mapharsen was given in only 10 cubic centimeters of solution.

Probably the most important factor in treating relapsing fever is the timing of the arsenical injection. It is generally agreed that the most opportune time is at the beginning of the attack, that is, within two days of the onset of fever. Experience in these cases was in accord with this dictum. It was soon learned that injections given near the time of the crisis invariably resulted in profound changes regardless of the dose of the drug. In some cases, an extreme pyrexia, 108° F. and above, followed the injection. This was usually accompanied by terminal convulsions. The more common reaction consisted of a transient rise in fever followed by deep medical shock which frequently progressed to death in spite of all treatment. In general, it was found that the nearer the arsenical was given to the crisis, the more severe the reaction.

Several patients were admitted in a critical condition even though, according to the history, they had been ill only one or two days. Most of these patients had an extreme pyrexia, 106° F. and above, but a few were in a state of circulatory collapse. Mapharsen given to these patients invariably made them worse. After this lesson was learned, mapharsen was withheld until the subsidence of the attack and was administered at the beginning of the next attack, at which time it could be more safely given. Treatment of these patients during the critical period was entirely supportive.

The treatment of patients in circulatory collapse was the same regard-

less of whether it appeared following mapharsen or in the natural course of the disease. Intravenous plasma, saline and glucose solutions were given along with local heat and stimulants such as caffein. In spite of intensive supportive therapy the response was usually slow and the majority of these patients died following a progressive pulmonary edema.

Twelve cases (9 per cent) gave evidences of mild toxic reactions to mapharsen. A toxic reaction was thought to have occurred in those patients who developed symptoms and signs not present prior to the injection. There were four instances of mild nausea and vomiting, four of a profuse diarrhea, and four instances where nausea, vomiting, and diarrhea were present. All of these reactions occurred following the first injection of 0.06 gram of mapharsen. With the reduction to 0.04 gram of mapharsen, no further toxic reactions were noted. In addition to the cases mentioned above, there were four patients who had violent chills and fever immediately following the injection. Though these cases might be included in the group of toxic reactions, it was not possible to determine whether this was an attack induced by the destruction of large numbers of spirochetes or a toxic reaction to mapharsen. Because of the absence of nausea and diarrhea, it was felt that an induced attack was more likely.

Results of Treatment. All of the 134 patients received one or more injections of mapharsen.

Under ordinary circumstances, a disease such as relapsing fever supplies the ideal medium for measuring the efficacy of specific treatment. Results can be measured in terms of complete recovery or death. However, the presence of other factors such as the nutritional state, concomitant diseases, and a heavy incidence of past diseases will alter, to a considerable extent, the final results. These factors, plus a certain degree of inexperience on the part of those handling these cases, undoubtedly contributed to the mortality rate in this epidemic.

Mapharsen proved to be a very effective drug against relapsing fever. In the entire series, only in two cases were spirochetes found after its use. Both of these cases had tremendous numbers of the organism in the initial smear and both were in a critical condition. In spite of this, a second injection resulted in a prompt recovery in both instances. Toxic reactions were infrequent and were of no consequence in the outcome of any case.

The use of multiple doses of 0.04 gram of mapharsen given three to five days apart was found to be the best method of treatment. Using this plan, the recurrence rate was reduced to practically nil, and toxic reactions were not observed.

In general, convalescence was rapid following mapharsen. In a few days, recovery was complete. Because of the crowded conditions of the hospital, most cases were returned to duty somewhat sooner than was desired, but even in the short period of their hospital stay, a remarkable change was usually seen. The average patient gained several pounds on the solid U. S. Army ration. Routine vermifuges were followed by iron and multi-

vitamin therapy with a visible improvement in vigor and general well-being. One patient, who was retained for duty in the hospital, gained over 30 pounds in six weeks.

Complications. The chief complications attributable to relapsing fever were hemorrhage, hepatitis, conjunctivitis, deafness, orchitis, and myelitis. Occurring concomitant with relapsing fever were seven cases of malaria, four of louse-borne (OX–19) typhus, one of smallpox, two of lobar pneumonia, and two of rheumatic heart disease.

Hemorrhage was the most common complication. It was seen in 16 cases (12 per cent). Epistaxis and hemorrhage from the bowel each occurred in six cases, hemoptysis was seen in three patients, and hematuria in one. In two cases, epistaxis was of a serious nature. Both had been bleeding intermittently for two days prior to admission. One succumbed from shock incident to blood loss. The other required tight nasal packing for two days, but made an uneventful recovery. It is likely that these two cases were precipitated by the high altitude flight which they made, as bleeding began during the flight. The remaining four cases of epistaxis occurred during the febrile attacks and were of no consequence.

Hemorrhage from the gastrointestinal tract was present in six cases. In two, it was deemed part of the hemorrhagic diathesis incident to severe jaundice. The other four cases were unexplained. Large amounts of bright red blood were passed in the stools of three cases and tarry stools were found in another. Hemorrhage from the gastrointestinal tract proved to be a bad omen, as four of the six cases were fatal.

The single case of hematuria was seen in an intensely jaundiced individual who also bled from the bowel and had purpuric areas over the extremities. The hematuria was gross and persisted over a period of three weeks. This patient made a slow recovery following mapharsen, vitamin K, and transfusions.

Fifteen cases (11 per cent) of icterus occurred in the series. The jaundice varied from mild to intense and was of the nonobstructive type. Concomitant hepatomegaly was present in all cases and the findings were thought to represent an inflammatory hepatitis produced by the *S. recurrentis.* When present, this complication was usually seen at the time of admission, though two cases developed during convalescence. The disease was fatal in two instances. One patient grew progressively more jaundiced, had profuse hemorrhage from the bowel, and developed purpura of the dependent areas of the entire body. Death followed a short period of coma. The other fatal case also died in coma but did not exhibit any unusual bleeding tendency. The course of the hepatitis was not influenced by mapharsen. It tended to remain for 10 to 20 days with gradual recovery.

A purulent conjunctivitis resembling Koch-Weeks infection was encountered in 11 cases (8 per cent). In two of these, Koch-Weeks bacilli were identified on smear. All cases responded satisfactorily to local sulfonamide therapy. It was not determined if this was a true complication of

relapsing fever or an incidental infection. As conjunctivitis was seen only in the Chinese with relapsing fever, it was interpreted as a true complication.

A rash was found in only six cases (4 per cent). It consisted of a purpuric macular eruption most prominent on the trunk with scattered lesions on the extremities. A concomitant lymphadenopathy was not noted. In each of these cases, typhus was suspected, but was ruled out by agglutination and therapeutic response to mapharsen. The rash remained for four to five days before fading.

The two cases of orchitis appeared suddenly in the form of rapid swelling of the testicle. Both appeared during the febrile paroxysm and both subsided spontaneously within a week.

One of the most interesting complications in the series assumed the form of a mild myelitis in two cases. It was manifested by motor and sensory changes in the lower extremities and was of a very transient nature. The spinal fluids, though clear, showed increased pressure, a positive Pandy test, and a lymphocytic pleocytosis. Spirochetes were not seen in the spinal fluid. No special treatment other than nursing care was required and recovery was complete within three weeks in both cases. It is possible that the marked weakness in the legs seen after the crisis may be on the basis of a low-grade myelitis. Unfortunately, spinal fluid studies were not done on cases other than these two.

Eight patients (6 per cent) developed parotitis. It usually appeared shortly after recovery from the crisis during the period of convalescence. Both glands were involved. On palpation, they were soft and doughy in consistency. No tenderness or other signs of inflammation were present. The openings of Stenson's duct appeared normal and expressed secretions clear. Parotitis was not accompanied by an exacerbation in fever in most cases. It was in no way affected by a second arsenical injection. Parotitis was thought to be a sequel to general debility and poor oral hygiene rather than a true complication of relapsing fever.

Transient deafness was present on admission in six cases. This may well have been an effect of high altitude flying. In no instance did this complication persist and no special treatment was required.

Fatal Cases. Previously reported epidemics have given a variation in mortality of from 2 to 50 per cent.[4] Sixteen cases (12 per cent) of the 134 cases in this series, died following treatment with mapharsen. At first glance this figure may seem high, but when the factors mentioned above are considered, it appears, in fact, lower than would be expected. This view is supported by statistics obtained from the Indian camp. A report from that camp stated that 50 per cent of the recruits were ill at the time of arrival from China. The average mortality among recruits hospitalized from whatever cause was slightly above 10 per cent. These figures demonstrate very well the poor condition of the group as a whole.

The cause of death could not be accurately determined because of the

inability to obtain postmortem examinations. Descriptions of the causes of death are, therefore, in clinical terms.

Of the 16 fatal cases, eight died in a state of circulatory collapse, three in coma, two of convulsions and hyperpyrexia, two following severe hemorrhage, and one as a result of a secondary parotitis.

The circulatory collapse appeared shortly after the termination of the febrile attack and proved very refractory to treatment. It strongly resembled the so-called secondary shock.

Summary and Conclusions

1. The clinical findings and complications in 134 cases of Asiatic relapsing fever due to *S. recurrentis* have been briefly presented and discussed.

2. Mapharsen was administered to all cases and proved to be an effective drug. The best results were obtained when two injections, each 0.04 gram, were given three to five days apart.

3. The mortality of 11.9 per cent was offset by the poor general condition of the patients.

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CYSTIC DISEASE OF THE LUNG *

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Cystic disease of the lung has long been considered a rather uncommon condition, probably because it rarely gives symptoms and is usually found in the course of routine physical and roentgen examinations. The roentgenograms made routinely at the army induction centers will undoubtedly uncover a great number of hitherto unsuspected cases because these are surely more common than is generally believed.

Recently we had the opportunity to study such a group, many of whom presented the various complications of this disease. Since the literature dealing specifically with the complications of this condition is rather meager, we feel that this report is justified.

No discussions of the cystic diseases of the lung appeared in the American literature until 1925, when Koontz [1] reported a case with an autopsy record and reviewed the foreign literature. Most of the papers since then have dealt with individual case reports and attempts to explain the pathogenesis and pathology of the disease; only since 1935 has any extensive number of cases been reported. The term "cystic disease of the lung" is rather loosely used in the literature. From the examination of many available reports, we feel that cystic disease of the lung may be defined as *any condition in which the lung parenchyma is replaced by sharply defined cavities containing fluid or air.* In order to simplify the discussion we are excluding dermoid cysts of the lung, ecchinococcus cysts and encapsulated interlobar accumulations of fluid or air. It is generally agreed that cystic lung disease may be congenital, acquired or both, although the prevalent opinion seems to lean to the congenital origin. Both forms have been termed "honey-combed lung" and "cystic bronchiectasis" when the cyst wall contained bronchial components, and "pneumatocele" or "pneumocyst" when the cyst wall resembled bullous emphysema.

From a clinical and pathological point of view, congenital cystic disease falls into two main groups. The first is the large solitary cyst which may occupy one or more lobes, often displacing the heart and mediastinum to the contralateral side. Such cysts compress the surrounding parenchyma and are usually found in infancy and early childhood, giving symptoms of cyanosis and dyspnea, accompanied by physical signs of a tension pneumothorax. These solitary cysts are lined by a layer of columnar and cuboidal epithelium, resting on a tunica propria and a layer of connective tissue. No

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doubt all these cysts communicate with a bronchus, but this communication is very difficult to demonstrate grossly. However, careful serial section of many of these cysts will disclose the communicating bronchus. In the case of Koontz,[1] several communicating bronchi were found in the examination of 50 serial sections. Definite bronchial communication must exist if the cyst is to remain open, since complete bronchial occlusion and failure of ingress of air will cause obliteration of the cyst through the absorption of the trapped air. Cheney and Garland [2] have reported such a congenital cyst in an adult girl 19 years of age, giving the patient no symptoms whatsoever despite the fact that her vital capacity was only 27 per cent of the expected normal. Similar cases have been reported by Wood,[3] Eloesser,[4] Kirklin,[5] Sharpe,[6] and Ford.[7]

The episodes of respiratory difficulty seen in these patients have been ascribed to progressive enlargement of the cysts with the development of positive intraluminary pressure and the displacement and herniation of the mediastinum, or to localized spontaneous pneumothoraces as the cysts rupture under the strain of positive pressure. Soon, however, the rent in the visceral pleura overlying the cyst wall heals and the cyst lumen again enlarges.

Roentgenologically these cysts appear as large areas of radiolucency which may or may not contain fluid. As a rule, the cystic spaces are well defined and are frequently traversed by linear strands of trabeculation. When the cyst cavities are ballooned out by the highly positive intraluminary pressure, the trachea, heart and mediastinum may be displaced into the contralateral hemithorax and a marked resemblance to a tension pneumothorax will be apparent.

The second form of cystic disease which is apparently congenital is one in which the lung parenchyma is replaced by areas of cystic degeneration ranging from multiple miliary cysts scattered throughout lung parenchyma to large multilocular or unilocular cysts occupying one or more lobes. These cystic cavities are lined by cuboidal or columnar epithelium which may be thrown into folds by intraluminary proliferation giving rise to an adenomatous appearance. Between these two extremes intermediate forms may be encountered giving the lung tissue a spongy appearance, it being made up of clusters of thin-walled cavities varying in size from 1 to 3 cm. These cavities communicate freely with bronchi and are lined with columnar ciliated or non-ciliated epithelium and show the usual architecture of a bronchus—smooth muscle, cartilaginous rings and mucous glands being found in the cavity wall on histologic examination.

Radiographically this form of cystic disease is characterized by the honeycombed appearance of the pulmonic fields, the lung structure showing a large number of thin walled, sharply defined annular shadows without accompanying interstitial parenchymal infiltration. This roentgen appearance is especially diagnostic when the lesions are in the upper lobe, are bilateral, and there is no distortion of the thoracic cage or retraction of the mediastinum as seen in the acquired forms of bronchiectasis. However, when infection

is superimposed on a congenital lesion it may be difficult to distinguish from the acquired form by roentgen examination. The direct communication with the bronchus as indicated above can be demonstrated on bronchography and the grape-like clusters of cystic spaces will be found to stand out.

Acquired pneumatocele or cystic disease is usually associated with respiratory infection, chronic bronchitis or peribronchitis, pulmonary fibrosis and emphysema, or bronchial asthma. It is evident that any pathologic lesion

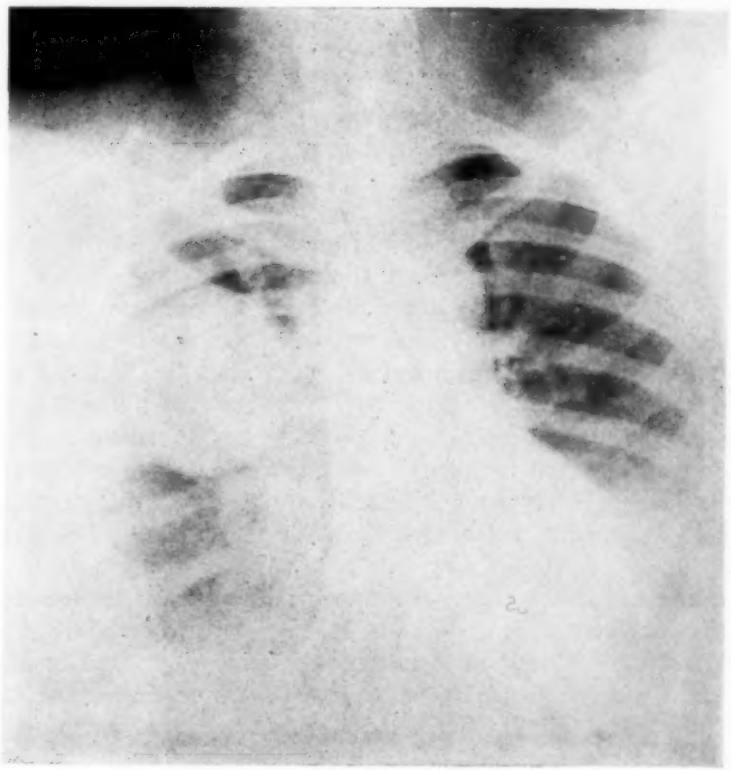

FIG. 1. *Case 1.* Fluid filled cyst. Note round, sharply defined density distinct from mediastinal structures. This shadow represents a congenital cyst of the lung which has not extruded its fluid contents and demonstrates a step in the pathogenesis of the disease.

causing incomplete bronchial obstruction will be followed by obstructive emphysema with distention of the corresponding alveolae and thinning with resultant final rupture of the alveolar septa. Bleb and bulla formation is the inevitable result, especially if the stenotic lesion is such that a check-valve mechanism acts at the bronchial orifice.[8, 9, 10] Pathologically, the acquired form of cystic disease is indicated by the presence of coal pigment in the contiguous alveolar walls and by the existence of blebs and bullae at the periphery of the lung. Lesions of this type may be seen even in infancy and childhood and may disappear when the endobronchial lesion heals and, as a matter of fact, cases of this type were reported by Caffrey.[11]

Roentgenographically, acquired pneumatocele presents itself as a poorly defined annular shadow devoid of pulmonary markings. Close scrutiny will show fine linear bands traversing the cystic space. This, too, is to be distinguished from localized pneumothorax. It is obvious, then, that from a roentgen and clinical point of view, it may be very difficult to distinguish the acquired from the congenital form of solitary cyst described above. The fact that most cases of the latter die in infancy and early childhood makes one suspect an acquired etiology when this lesion is seen in an adult. However, Kirklin[5] and Cheney and Garland [2] have described cases in adults who had large solitary cysts with ballooning and herniation of the mediastinum.

Roentgenographically, the differential diagnosis from a localized pneumothorax may be made by the establishment of a diagnostic pneumothorax when the cyst wall will be separated from the thoracic cage and its cystic nature will become discernible. Again, the introduction of a pneumothorax needle into the cyst lumen and the measurement of the intraluminary pressure manometrically before and after the aspiration of a given volume of air, will also help to establish the differential diagnosis. Removal of air will alter intraluminary pressure very little in cystic disease, whereas well defined changes in the intrapleural readings will take place in localized pneumothoraces. As stated earlier, bronchial connections are difficult to demonstrate macroscopically; hence, bronchographic examination will fail to visualize contrast medium in the cyst space. However, compression of the surrounding lung parenchyma will bunch the bronchi in the vicinity of the cyst. Case 12, showing a large pneumatocele, illustrates this point very nicely.

The pathogenesis of congenital cystic disease is very interesting. The most plausible explanation is as follows: It will be remembered that the lungs are formed from the lung buds whose ends become lobulated at about the fourth week of embryonic life, there being three lobules formed on the right and two on the left. These lobules undergo dichotomous branching, the terminal portions of the branches becoming expanded to form atria. At about the sixth month, the alveoli are formed as evaginations from the latter. If the process is arrested early, during the early subdivisions, large solitary cysts may be formed. If the process is arrested later in embryonic development, multiple cysts will result. It will be remembered too, that the thoracic cage grows much faster than its contents. If then no pulmonary alveoli are formed and the development of the bronchopulmonary segment does not keep pace with the increased capacity of the fetal thorax, dilatation of the involved bronchi will follow; case 4 illustrates this point very well. The lateral view shows the huge dilated bronchi with cyst formation.

Another factor which very likely plays a part is the fact that there may be an arrest in the development of the bronchiole in the tube stage. Excretion of mucus from the glandular elements of the bronchiolar wall may form fluid-filled sacs. When the intraluminary pressure rises the sac may rupture

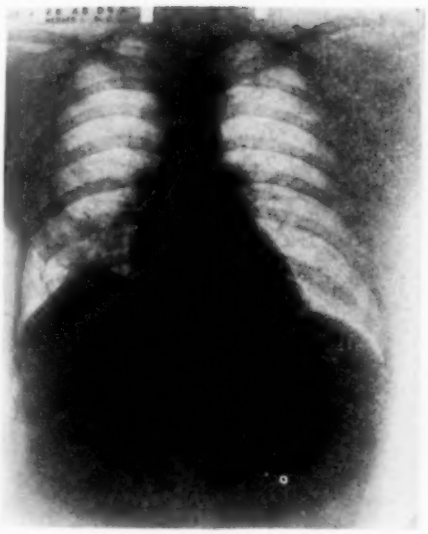

FIG. 2.

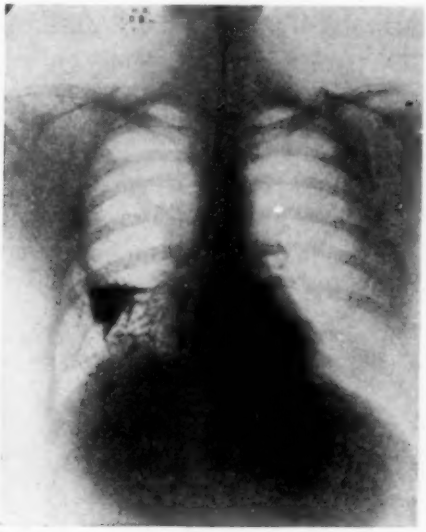

FIG. 3.

FIG. 4.

FIGS. 2, 3, and 4. *Case 3.* Congenital cystic disease complicated by hemorrhage. Roentgenogram of chest showing area of diminished illumination of right lower lung field and tenting of right diaphragm due to pulmonary fibrosis and pleural thickening from previous pneumonitis and empyema. Frequent episodes of hemoptysis suggested bronchograms, figures 3 and 4, demonstrating large cysts filled with contrast medium.

and its contents empty into a bronchus. Air now enters the cystic space and it in turn dilates, especially if the mechanism at the bronchial orifice is of the check-valve or bi-pass variety. Credence is given to this theory by the presence of fluid-filled pulmonary cysts which never give rise to symptoms and are only discovered as incidental findings during routine roentgen examinations as seen in case 2.

The most plausible theory of the pathogenesis of the acquired form of cystic disease has been discussed above. In addition, it has been suggested by Wolbach [12] and by Rabinowitz and Rogers [13] that vitamin A deficiency may cause the accumulation of keratinized epithelial cells in the bronchial

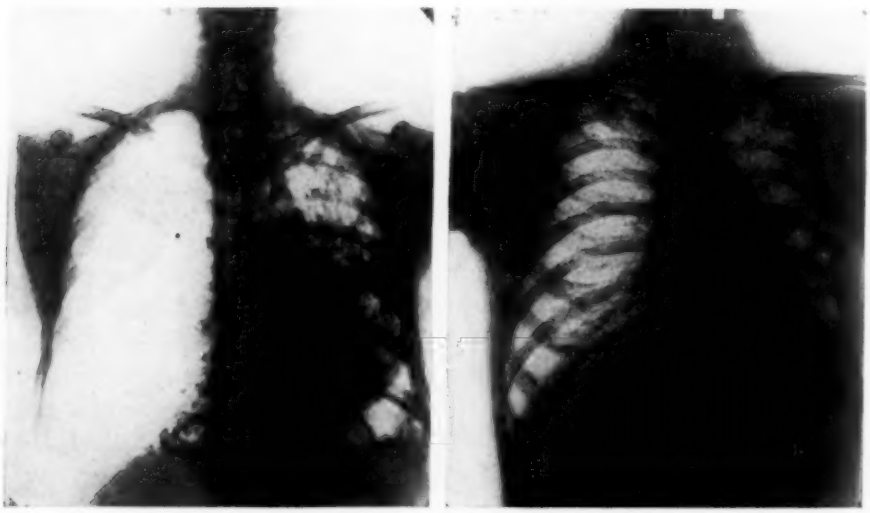

FIG. 5. FIG. 6.

FIGS. 5 and 6. *Case 7.* Cystic disease of the lung complicated by infection. Figure 5 shows bucky exposure of the chest during attack of pneumonitis. Trachea, heart and mediastinum are deviated to the left. Numerous annular shadows can be visualized in the left upper lobe. Figure 6: Under chemotherapy, pneumonitis subsided and thin-walled annular shadows can be visualized above the third anterior rib. Note how difficult it is to distinguish this case from that of the acquired disease.

lumen, causing in turn obstructive emphysema and cyst formation. The diet in all cases observed by us was certainly adequate and it is difficult, therefore, for us to incriminate a vitamin A deficiency.

It is well to keep in mind that cystic disease of the lung (uncomplicated) rarely gives rise to symptoms. Aside from the large solitary cysts which balloon out under the influence of a check-valve mechanism at the bronchial orifice and are fatal early in life, cystic disease seldom gives symptoms. Only after close questioning will the patients divulge the fact that they have had a non-productive cough which is not at all distressing. However, upper respiratory infections are very often followed by infection in the cystic areas and episodes of pneumonia are obtained from many of the histories.

The severe constitutional symptoms associated with acquired bronchiectasis are not seen in these cases; neither are the cerebral manifestations associated with pulmonary suppuration. As age increases and cardiorespiratory reserve diminishes, the patients often complain of increasing dyspnea; in fact, death from right-sided heart failure is not uncommon. Routine physical or roentgenographic examinations usually establish the diagnosis. However, complications of this disease are common and some of these bring the patient to the attention of the doctor. Probably the most frequent of such complications is hemorrhage, occurring in four of our 13 cases. The hemorrhage is seldom profuse, although in case 5 it was of exsanguinating proportions, necessitating repeated transfusions on several occasions. It is, indeed, noteworthy that the literature fails to emphasize hemoptysis as an important symptom; Kirklin [5] even goes so far as to state that it is rare. On the other hand, cases reported by Smith,[14] Hennel,[15] and Churchill [16] presented hemorrhage as the main complaint. The true source of the hemorrhage has not been definitely established. Case 5 had her hemoptysis following febrile episodes associated with pneumonitis in the surrounding lung parenchyma. It seems that infection in the cyst wall eroded a bronchial or pulmonary blood vessel and thus caused the hemorrhage. However, cases 2 and 3 had hemoptyses without antecedent infections. Perhaps blood vessels coursing in the cyst wall, unsupported on their luminary side, are prone to rupture under the strain of increased intrapulmonic arterial pressure.

The next complication in order of frequency is infection with surrounding pneumonitis; this occurred in two cases of our series. In each case the infection ran a protracted course and gave a sulfonamide response. It is worthy of note that in case 6 an attack of pneumonia caused the patient to be examined by a physician and thus the true nature of the underlying condition became apparent.

The third complication encountered in our series was spontaneous pneumothorax. This is clearly brought out in case 9, whose spontaneous pneumothorax complicated congestive heart failure. Only after this complication was truly evaluated and the appropriate therapy instituted was the patient benefited.

Case 8 developed a spontaneous hemopneumothorax as a result of bilateral apical emphysematous bullae which were probably congenital in origin. No evidences of parenchymal fibrosis of tuberculous or any other origin could be found. The rupture of a vascular adhesion secondary to the pneumothorax was probably the origin of the bleeding.

Acquired cystic disease was discovered incidental to examination for food handlers certificates as in case 11, during routine cardiac teleroentgenography in case 10, and while in search for a cause of progressive dyspnea in case 12. Particularly interesting is case 5, in that repeated attempts to demonstrate bronchiectasis by roentgenogram, bronchography and bronchoscopy were unsuccessful. A differential diagnosis from bronchial adenoma had to be

considered. Finally, laminography by H. K. Taylor of New York City demonstrated the true nature of the condition, i.e., cystic disease.

Case 1 is presented to show the pathogenesis of congenital cystic disease. Here a large round density was found in the right lung field during routine periodic health examination. It had been present for at least five years without any increase in size and had caused no symptoms. The patient refused to allow us to aspirate the cyst and we did not press her because we felt that it might be dangerous to do so. Such masses must be distinguished from solid lung tumors, especially teratomata, neurofibromata and carcinomata. The duration of the lesion and its sharply defined outline militate against these diagnoses. Moreover, its radiographic appearance, as a parenchymal density, well circumscribed, slightly less radio-opaque than the opacity of the cardiac shadow, and separated from the latter, fits in well with the diagnosis of cystic disease of the lung.

Case Reports

Fluid Filled Cystic Disease

Case 1. M. J., a 38 year old colored female, was first seen by one of us in 1940, when a physical examination was made for a health card as a domestic. She had no physical signs and no complaints. During routine fluoroscopic examination a large, sharply defined annular shadow presented itself. Since the patient had no complaints and refused any other diagnostic procedures, no attempt was made to aspirate the mass or remove it. The patient was later seen on two occasions in addition to the original examination; she was apparently perfectly well and the roentgen shadow was essentially unchanged. We believe that this shadow is due to a congenital cyst of the lung which has not extruded its fluid contents.

Cystic Disease Complicated by Hemorrhage

Case 2. E. J., a 22 year old colored male, entered the hospital in November, 1942, following hemoptysis of one quart of bright red blood. Past history was negative except for pneumonia at ages of 18 months, seven, nine, and 10 years. At the age of 11, the patient was admitted to Glen Gardner Sanatorium with a diagnosis of chronic pulmonary tuberculosis. He remained there a whole year and was discharged with a diagnosis of lung abscess of the right middle lobe. Physical examination was entirely negative except for the chest which showed dullness and diminished breath sounds in the right middle lobe. Roentgenograms disclosed an annular shadow in the right lower lung field with a dense wall and a fluid level. Lateral view proved this shadow to be in the right middle lobe. Subsequent lipiodol instillation confirmed the contention that this shadow was a large congenital cyst, freely communicating with a bronchus. The patient was advised to have a right middle lobectomy, but refused.

Case 3. M. L., a 29 year old white male, was first seen by us on November 13, 1943, complaining of right sided chest pain. The patient had apparently been well until the age of nine, when he had several small hemoptyses of three ounce quantities. At the age of 12 he had an attack of pneumonia complicated by empyema, necessitating several rib resections. The patient was hospitalized at this time for nine months. Even during his hospital stay he had two pulmonary hemorrhages. The patient fared very well thereafter, having only vague pains in his right chest on change of weather.

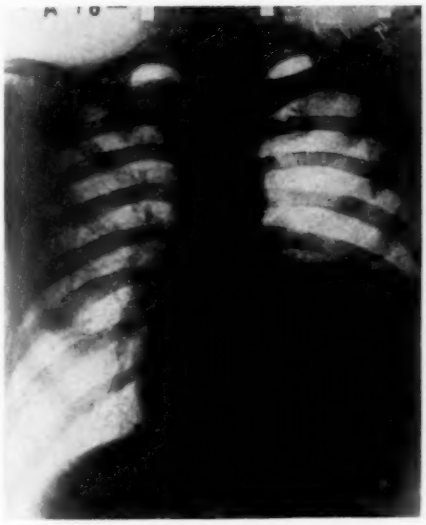

FIG. 7.

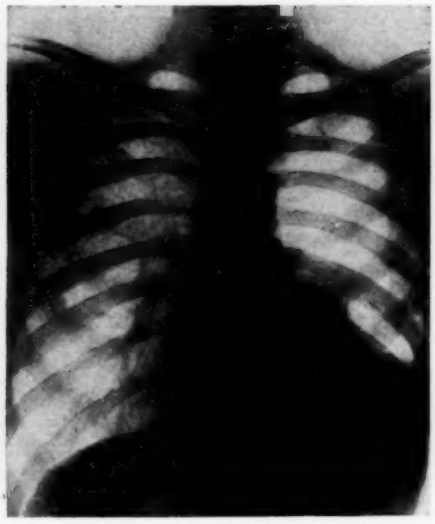

FIG. 8.

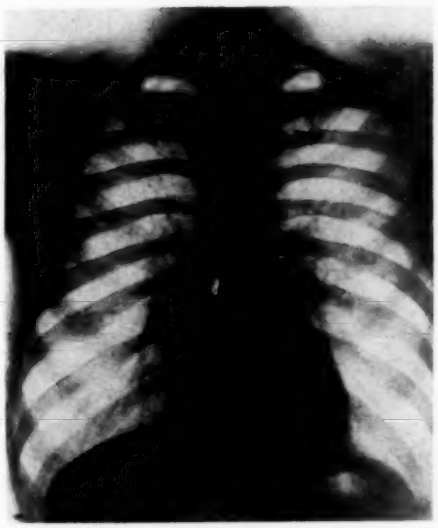

FIG. 9.

FIGS. 7, 8, and 9. *Case 8.* Cystic disease complicated by spontaneous hemopneumothorax. Figure 7 shows left hydropneumothorax with fluid level at the fourth anterior rib. There is some shift of the trachea, heart and mediastinum to the right. Several emphysematous bullae may be visualized at the extreme apex of the right upper lobe. Figure 8: After aspiration and oxygen lavage, the lung reëxpanded. Fluid proved to be frank blood which did not coagulate on standing. Figure 9: Lung completely reëxpanded, emphysematous bullae may be noted at the extreme apices.

At this time positive physical signs were limited to the chest where dullness and diminished breath sounds were found over the right lower and middle lobes. He was seen periodically and treated symptomatically. In June, 1943, the patient was inducted into the Army and during his basic training another hemoptysis occurred, this time amounting to about one pint. He was hospitalized and finally discharged with a diagnosis of bronchiectasis. He again returned to us for further studies. A lipiodol instillation into the right middle lobe showed a large cystic cavity which occupied the greater part of the right middle lobe and only now the true nature of his disease became evident. Figures 2, 3 and 4 show the ease with which the lipiodol entered this cystic cavity.

Case 4. S. G., a 34 year old white female, was first examined by one of our group on March 13, 1945, complaining of ready fatigue and pain in the upper anterior chest for the past two weeks. The patient had been well for eight years prior to this time, when she had a pulmonary hemorrhage of about two ounces. She had no premonitory signs and felt perfectly well for the succeeding two years when she had another hemoptysis. Since then she had repeated bleedings at two year intervals. In the interim there had been no cough, expectoration, chills or fever. The patient never experienced the symptoms of pneumonitis. The last hemoptysis occurred two years prior to this examination. Past history was unimportant with the exception of typhoid fever in 1918. The positive physical signs were limited to the chest; here there was a slightly tympanitic percussion note in the left upper lobe with diminished breath sounds and occasional medium moist râles. Roentgen examination showed an area of increased illumination occupying the left upper lobe in which lung markings could be made out only at the periphery. At the level of the anterior third rib, a definite annular shadow could be seen. The cystic bronchiectatic nature of the disease was easily demonstrated on bronchography where the iodized oil flowed into the left upper lobe bronchus, revealing large dilated bronchi and annular cystic cavities. Obviously, the only cure for such a lesion is a left upper lobectomy.

Case 5. J. M., a 21 year old female, was seen by us for the first time on July 10, 1944, complaining of cough, fever, and hemoptysis of three days' duration. The patient was well until February 1933, when she developed chills, fever and a cough, productive of a thick greenish yellow mucus. A diagnosis of bronchopneumonia was made at this time and was said to have been corroborated by roentgenographic findings. The patient was ill intermittently with the same chain of symptoms for the next year and a half. She then returned to school, but complained of left-sided pleuritic pain aggravated by coughing on rare occasions. For the next six years she was perfectly well. However, in April, 1939, the patient had a pulmonary hemorrhage amounting to about eight ounces. She remained in bed for about one week during which time she had mild streaking. In July of the same year she had a severe hemoptysis, requiring frequent transfusions; her hemoglobin fell to about 40 per cent. At this time the patient was hospitalized for one month; roentgenograms showed an exudative lesion of the left hilus. Bronchoscopy failed to reveal any endobronchial lesion. This procedure was done for the purpose of eliminating papillary carcinoma or benign adenoma of the bronchus as likely etiologic factors. Bronchogram at this time was unsatisfactory. Finally the hemorrhage ceased; the patient regained her strength and was discharged. In October, 1940, and August, 1941, the patient again developed brisk hemoptyses; both of these followed acute upper respiratory infections with "chest" colds. Each time the patient was laid up for three weeks. In September, 1943, she again had a hemoptysis of four ounces; this followed an attack of chills and fever. At this time the patient came under our observation. Physical examination showed dullness, diminished bronchovesicular breath sounds in the left upper lobe with occasional râles in the left axillary areas above the fifth rib. Roentgenographic examination revealed an area of diminished illumination extending along the inter-

lobar fissure, which was interpreted as an area of pneumonitis or an interlobar effusion. The patient was given sulfonamides with absolutely no therapeutic response. After 10 days her temperature, which had been up to 103° F., came down to 99° F., and she improved subjectively. However, the shadow as noted above remained, finally clearing in about six weeks. Attempts to ascertain the true cause for the hemoptysis were now made; iodized oil instillation failed to reveal any bronchiectasis. Bronchoscopy again was done; no intrinsic disease could be found in the left bronchial tree. Since a small calcified node was seen at the left hilus and it was suggested that this may have eroded a branch bronchus, thus causing the bleeding, a laminography was done to establish whether or not this calcified node bore a definite relation to a bronchus. The patient was referred to Dr. H. K. Taylor of New York City, who took layer films; at the levels of 3¼"–4" from the anterior chest, definite cystic spaces were visualized and the true nature of the disease process was demonstrated.

Cases Complicated by Infection

Case 6. M. M., a 15 year old white female, was seen by us on September 3, 1942, complaining of cough and expectoration lasting three weeks. The patient was perfectly well until August 16, 1942, when she developed left-sided chest pain and a non-productive cough. Her temperature rose to 103° F., and was preceded by a severe chill. She was taken to Rockaway Beach Hospital, where a diagnosis of bronchopneumonia was made. The patient was given sulfonamides with but indifferent results, the temperature falling by lysis after 10 days. At the time of our observation on September 13, 1942, she felt weak and coughed with profuse expectoration which was mucopurulent, occasionally blood-stained, but always non-fetid. Essential physical findings were limited to the lungs where the percussion note was somewhat diminished over the left upper lobe anteriorly and the breath sounds diminished; an occasional rhonchus was audible over this area. Roentgenographic examination revealed an area of infiltration along the base of the left upper lobe representing an area of pneumonitis and interlobar effusion. In this region several annular shadows could be found, the lowermost of which contained a fluid level. Sputum and gastric contents were negative for acid-fast bacilli after repeated examinations. Culture of the sputum failed to show Friedländer bacilli and was positive for hemolytic streptococcus. The patient was given supportive treatment and improved. Bronchography failed to reveal any contrast substance in the cystic cavities, although the major bronchi draining the areas of the cystic spaces were visualized. The patient was seen on May 23, 1944; the cystic spaces were still apparent. The pneumonitis had completely cleared and the patient had no complaints.

Case 7. F. C., a 42 year old white clerk, was first referred to us on November 15, 1944, complaining of cough and expectoration of a non-fetid, mucopurulent sputum. His previous history disclosed four attacks of pneumonia; the first at the age of six, the second at 36, the third at 41, and the fourth at 42. The last one occurred in September, 1944. The patient during the last attack complained of an upper respiratory infection which gradually descended into his chest, as evidenced by chills, fever, left-sided chest pain, and marked increase of cough and expectoration. At this time he was hospitalized and treated with sulfonamides to which he gave a definite chemotherapeutic response. He spent his convalescence in Florida where he improved very much, gaining weight and noting marked diminution in his cough and expectoration. While he was there, lipiodol instillation was done and the patient presented this bronchogram at the time of his first visit. He now complained of cough, profuse expectoration and occasional night sweats. Physical examination revealed a rather emaciated, slight man, markedly plethoric. Essential physical findings were as follows: dullness over the entire left lung from apex to base; diminished bronchovesicular breathing over the whole left lung, with many medium and coarse moist

râles. No clubbing of fingers was noted. Fluoroscopic examination showed an exudative productive lesion involving the greater part of the lung structure on the left with many annular shadows occupying the upper half of the left lung; the trachea, heart and mediastinum were displaced to the left. The interspaces on this side are narrowed and the diaphragm elevated. On fluoroscopy there was a definite shift of the mediastinum to the left on inspiration and a return to former position on expiration. On a regimen of postural drainage and a high caloric diet and small doses of sulfonamides the patient improved, so that on March 10, 1945, the exudative process had entirely diminished and the areas of fibrosis and cystic bronchiectasis became apparent. We believe that this is an instance of cystic bronchiectasis complicated by repeated infection, making it very difficult to distinguish from the acquired form. The sharply defined annular shadows seen on the last roentgenogram without surrounding parenchymal infiltration, tend to confirm this opinion.

Cases Complicated by Spontaneous Pneumothorax

Case 8. N. G., a 31 year old white male, was first seen at his home complaining of sudden severe pain in his left chest; this was accompanied by marked pallor. The onset was about three days prior to this examination and, as stated above, was ushered in by severe left chest pain. The patient went to the Newark City Hospital, where his chest was strapped and then he was allowed to go home. Symptoms improved the following day; however, 24 hours after the initial episode, the pain recurred and the patient became extremely pale. Physical signs revealed a right hydropneumothorax with hyper-resonance and diminished breath sounds above the fifth posterior rib, dullness and absent breath sounds from there to base. He was admitted to the Newark Beth Israel Hospital where roentgenographic examination showed a right hydropneumothorax with displacement of the heart and mediastinum to the right. Chest paracentesis revealed a frankly bloody fluid which did not coagulate on standing. The chest cavity was emptied of this material and rapid reëxpansion performed by means of oxygen lavage. The true nature of the disease was now revealed, since roentgenographic examination showed several bullae at the apex of the left upper lobe with a similar lesion in the contralateral lobe.

Case 9. C. H., a 43 year old white male, was admitted to the Newark Beth Israel Hospital because of dyspnea and weakness. The patient had had symptoms of diminished cardiac reserve for one year prior to admission. For the last six months he had had attacks of nocturnal paroxysmal dyspnea and coughing. Physical examination revealed a poorly nourished man, orthopneic and dyspneic; neck veins were distended. There was cyanosis of the lips and fingernail beds with clubbing of fingers and toes. The heart showed its point of maximum intensity in the fifth space outside the midclavicular line; heart sounds were of fair tonal quality. A high pitched systolic murmur was heard at the mitral area. Pulse rate and ventricular rate were 120 per minute; blood pressure was 180 mm. Hg systolic and 130 mm. diastolic. Fine moist râles were noted at the lung bases. The liver was palpable four fingers below the costal margin. The patient was placed on bed rest, digitalized and given appropriate therapy for congestive heart failure; however, the dyspnea was unrelieved. Roentgenographic examination revealed the true cause of his respiratory difficulty; a large spontaneous pneumothorax presented itself. In the underlying lung parenchyma, several well defined annular shadows could be seen, clearly demonstrating the cystic nature of the parenchymal disease. After oxygen lavage the lung reëxpanded and the signs of failure promptly improved. The patient became subjectively well and was discharged from the hospital under digitalis medication. It is interesting to note that for the past three years he has been working as a barker in a circus.

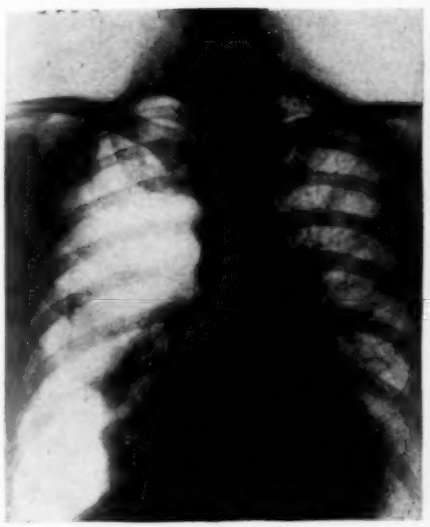

FIG. 10.

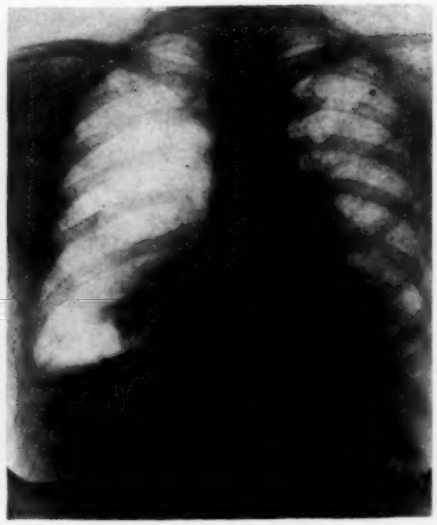

FIG. 11.

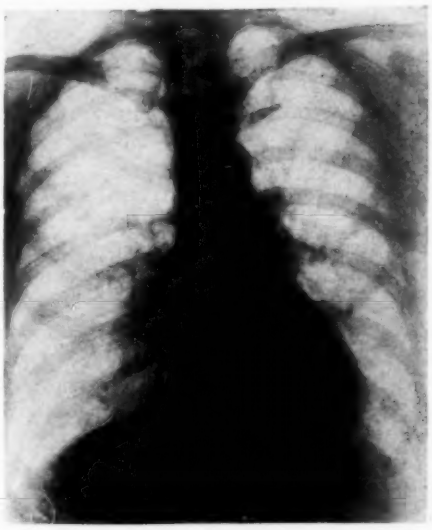

FIG. 12.

FIGS. 10, 11, and 12. *Case 9.* Cystic disease complicated by spontaneous pneumothorax. Figure 10 shows spontaneous pneumothorax in patient with hypertensive heart disease and congestive failure. Several thin-walled annular shadows may be seen in partially collapsed right upper and middle lobes. Figures 11 and 12 show reëxpanding right lung; the annular cystic spaces are better seen on original roentgenogram than in reproduction.

ACQUIRED CYSTIC DISEASE

Case 10. Ayerza's disease with acquired pneumatocele. C. G., a 41 year old Spaniard, was admitted to the medical service of the Newark Beth Israel Hospital in March, 1940, complaining of exertional dyspnea, orthopnea, marked cyanosis and swelling of both ankles of two years' duration. The past history is significant in that he had always been well until 1911, when he developed bronchial asthma with frequent episodes of respiratory difficulty. At the age of 22 the patient had a penile sore for which he received 12 intramuscular and 12 intravenous injections. However, despite this apparently inadequate therapy, his serologic reaction remained negative since 1925. His present illness began insidiously with increasing dyspnea, blue-black cyanosis, and marked orthopnea. Physical examination revealed the following pertinent findings: Scleral vessels were dilated and of a definite bluish hue. Pupils were equal and reacted to light and accommodation; fundi showed a marked degree of cyanosis and the retinal vessels were dilated. Cervical veins were distended but did not fill from below. Skin and mucous membranes were of an extreme purple color, evidence of the severe cyanosis. The chest was barrel-shaped and kyphotic. The percussion note was hyper-resonant throughout with diminished breath sounds and prolonged expiratory phase and many sibilant and sonorous râles. The heart was definitely enlarged; the point of maximum intensity was in the sixth space outside the midclavicular line. The sounds were of poor tonal quality; there were no murmurs; P_2 was greater than A_2; sinus rhythm was regular. The pulse and ventricular rates were 86 per minute and blood pressure readings were established at 164 mm. Hg systolic and 90 mm. diastolic. The liver was down three fingers'-breadth below the costal margin and the spleen one finger's-breadth. The extremities showed bilateral clubbing of the fingers and toes, marked cyanosis of the nail beds, and pitting peripheral edema.

Laboratory data: Hemoglobin 130 per cent, red blood cells 6,250,000, white blood cells 6,000 with a normal differential count. Venous pressure—13 cm. of blood. Blood and spinal fluid serologic reactions negative.

Electrocardiogram showed a right axis deviation; peaked P-waves in Leads II and III.

Roentgenographic examination of the chest showed evidence of bilateral emphysema with a large pneumatocele in the left lower lung field. The latter probably arose as a result of prolonged bronchial asthma, chronic bronchitis and peribronchitis, increased intra-alveolar pressure due to the failure of egress of air during expiration, rupture of alveolar septa and cystic formation. We believe that this case illustrates the usual sequence of events in the acquired form of cystic disease.

Under a régime of therapy for the congestive failure and frequent phlebotomies, the patient got along fairly well.

Case 11. N. B., a 35 year old white baker, was first seen at the chest clinic of the Newark Beth Israel Hospital on December 17, 1940. The patient was perfectly well until 15 years prior to this, when he noted an insidious onset of cough and expectoration of a thick white tenacious sputum, never foul smelling. He had no hemoptysis, night sweats, anorexia or weakness. The patient was referred to the Newark Board of Health, because of an abnormal shadow seen in his chest on routine fluoroscopy prior to obtaining a food handler's certificate. His past history is significant only in that he had frequent "colds" and asthmatic seizures during the past 15 years, with frequent attacks of allergic rhinitis and urticaria. Physical examination was negative except for the chest which showed generalized hyper-resonance and diminished breath sounds. An occasional rhonchus was heard in the right chest. Roentgenographic examination showed evidence of bilateral hyperillumination of the lung fields. A large thin-walled annular shadow could be seen in the medial portion of the right lung field. On bronchography, no contrast substance was found

to enter the cystic space. However, the bronchi in the surrounding lung tissue were visualized and bunched in the contiguous lung parenchyma. Diagnosis: Chronic bronchitis and emphysema with large pneumocyst in the right lower lobe.

Case 12. E. J., a 48 year old coal miner, was first seen by one of us complaining of frequent "colds" and asthma. The patient had a definite exposure to silica dust, having been a miner in Scranton, Pennsylvania, from 1920 to 1932. He had had a chronic hacking cough for 12 years, only occasionally productive of small amounts of phlegm. Recently, his cough had become worse and he noted dyspnea on exertion.

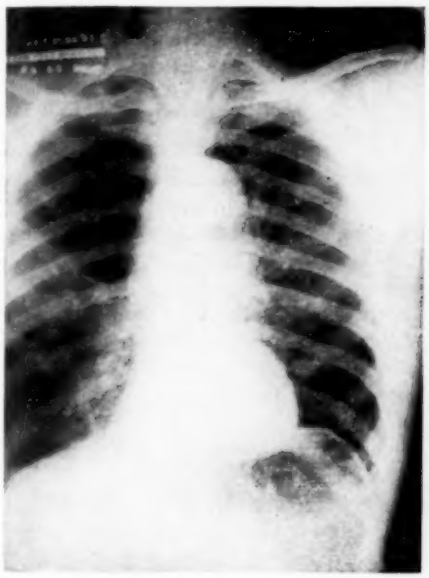

FIG. 13.

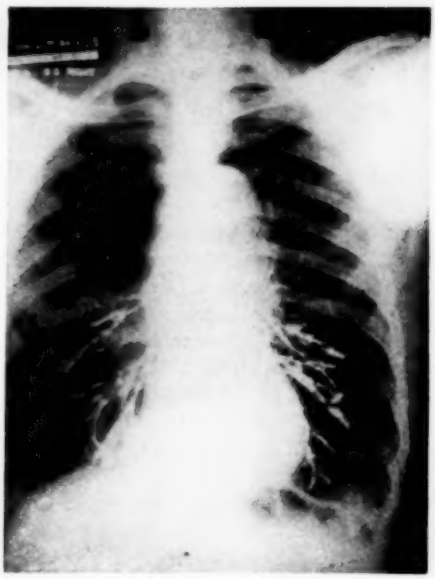

FIG. 14.

FIGS. 13 and 14. *Case 12.* Acquired cystic disease. Acquired pneumatocele in a silicotic coal miner. Figure 13 shows large pneumatocysts of right upper lobe, right lower lobe and left lower lobe; note absence of lung markings. An occasional trabecula could be seen coursing through the cystic area of the right lower lobe. In figure 14 bronchogram fails to show the contrast medium in any of the cystic areas. Cylindrical bronchiectasis may be seen bilaterally.

Physical examination was negative except for the following: There was slight clubbing of the fingers. The chest was definitely barrel-shaped with increase in the anteroposterior diameter. There was marked hyper-resonance to percussion bilaterally. Sibilant râles and wheezes could be heard over both lung fields with a few medium moist râles at the bases. The heart disclosed nothing of importance. Fluoroscopic examination confirmed by roentgenographic studies showed markedly brilliant illumination over the upper one-third of the right lung field. No lung markings could be visualized in this area; over the lower one-third of this same lung field another area of hyperillumination could be seen. On closer scrutiny, small strands traversing this cystic space were revealed. Intervening between both of these areas, a region of normal lung tissue with increased bronchovesicular markings was discernible. A similar area of hyperillumination could be seen at the left lower lung field. On bronchographic examination, no contrast substance entered either cystic space although the contiguous bronchi appeared dilated. Diagnosis: Obstructive pulmonary emphysema; emphysematous bullae; chronic bronchitis and peribronchitis; probable silicosis, although roentgen appearance not entirely diagnostic.

SUMMARY

Cystic disease of the lung may exist in the congenital and acquired forms. The pathology, pathogenesis, clinical and roentgenologic characteristics of each form are discussed. Cases illustrating steps in the pathogenesis of the congenital form (cases 1, 4), and its various complications—hemorrhage (cases 2, 3, 4, 5), infection (cases 6, 7), spontaneous hemopneumothorax (case 8), and spontaneous pneumothorax (case 9) are presented. The acquired form of the disease and its association with chronic bronchitis, peribronchitis, pulmonary fibrosis and bronchial asthma are illustrated in cases 10, 11, and 12.

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A BRIEF REVIEW OF ARTHRITIS AND ALLIED CONDITIONS IN TROPICAL DISEASES*

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MEN are being returned to the United States in increasing numbers from regions where they have been exposed to tropical diseases, hitherto largely unfamiliar to most physicians in this quarter of the world. Many of these diseases have already made their appearance in this country. Some, though not primarily classed as arthritides, present joint phenomena as part of their symptomatology. Many others have painful manifestations in various parts of the body, including the limbs. A description of such phenomena as they occur in tropical diseases may be of aid in diagnosis and in their differentiation from the better known diseases of joints as seen in temperate climates.

Arthritis is well known as a complication of a few tropical diseases and may occur, though less commonly, in many others. In the former group are bacillary dysentery, fungus infections such as coccidioidomycosis and Madura foot, filariasis and undulant fever. Somewhat less frequently one finds arthritis in patients with yaws, bejel, relapsing fever, rat bite fever, sporotrichosis, histoplasmosis, leprosy, smallpox, scurvy, tropical ulcer, dracontiasis and onchocerciasis. A few diseases practically never have associated arthritis. These include amebiasis and the leishmania infections.

Apart from definite arthritis, aches and pains in the joints are common in a wide variety of tropical diseases. In addition, in certain groups of diseases, notably the rickettsial, the viral and the spirochetal diseases, pains in the limbs, together with headache, backache or generalized body pains are so severe and so regularly present as to be of frequent assistance in diagnosis.

We exclude from the present discussion such diseases as tuberculosis, typhoid fever and the venereal diseases as well as the vitamin deficiencies, since they are prevalent in temperate climates as well as in the tropics.

Among the viral diseases, *dengue* is outstanding as a cause of pain. As part of a picture that includes severe generalized aches and pains, dengue may give pain in all of the larger joints, most intense in the knees, hips and back. Actually, it is the tendinous insertions about the joints which are the painful points rather than the joints themselves, and passive motion is painless. The pains appear with the rise of fever, often decrease as the fever diminishes and recur when the temperature again rises. Such pains appear in over 50 per cent of the patients and are often intense enough to merit the name "break-bone." There is usually no inflammation in the affected joints, though a few patients may show periarthritis of the knees or ankles which

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may persist for months. Walking may be difficult and stilted and pains in the hands and soles may continue for many weeks. In the end complete recovery is the rule.

The symptoms of *sand-fly fever* are similar to those of dengue.

Yellow fever does not usually present evidence of joint involvement. However, severe pains in the limbs, neck and back along with intense headache are often characteristic at the onset and may increase in succeeding days.

Serous or purulent arthritis has been described as an occasional complication of *smallpox*. In a few cases, ankylosis has occurred with resulting deformity. Generalized pains, including headache and pronounced backache, are characteristic.

Generalized pains are present in both *psittacosis* and *Rift Valley fever* and, in the latter, affect the back, shoulders and legs particularly.

Among the fungus infections *coccidioidomycosis* is a disease of special importance in the United States. Rosenberg [3] and his associates have summarized our recent knowledge of coccidioidal arthritis. The main reservoir of this infection in the United States lies in the Sacramento-San Joaquin Valley in Southern California. About 90 per cent of the cases reported in this country have been observed in California. The disease is caused by the fungus *Coccidioides immitis*.

Involvement of joints may occur in either the acute benign phase of the disease or in the more dangerous chronic granulomatous stage and in either phase any joint of the body may be affected. In the benign stage the disease is also known as "Valley fever," "desert fever," or "desert rheumatism." This syndrome is usually mild and is often characterized by an acute onset with malaise, general aches and pains, fever, sore throat, toxic erythema and occasionally conjunctivitis and bronchopneumonia. Signs of acute arthritis occur in about one-third of all patients with Valley fever, usually appearing simultaneously with the development of lesions resembling erythema nodosum. The affected joints are tender and painful on motion and are sometimes swollen. There is no effusion or suppuration, and residual damage or deformity does not occur. In fact, although there may be considerable pain, arthritis in Valley fever is relatively insignificant and in most instances subsides completely.

Involvement of joints in the granulomatous phase of the disease is a serious affair, usually the result of a disseminated infection which may lead to death. In not more than one out of 100 patients does Valley fever develop into this more serious chronic granulomatous form, the mortality of which may be as high as 50 per cent. Bone and joint lesions are fairly common. The roentgen findings may mimic those of tuberculous arthritis, with early destruction in the region of the articular surfaces and swelling of the overlying soft tissues. The joint space may be narrowed and the articular cartilage destroyed. In the later stages the joint space may completely disappear and ankylosis result. The arthritis in these cases is predominantly destructive with little tendency to heal by production of bone.

Destruction is usually more rapid than in tuberculosis. The joint involvement is commonly an extension from adjacent bony lesions. No specific treatment has been shown to be of value.

Histoplasmosis is caused by a fungus, the *Histoplasma capsulatum* of Darling. It is a generalized disease with variable clinical characteristics, including fever, enlargement of the liver and spleen, anemia, leukopenia, adenopathy and pulmonary symptoms. The initial manifestation is sometimes a small skin lesion which may develop into a generalized ulceration.

Key and Large [2] have reported histoplasmosis involving the knee joint clinically resembling tuberculosis. In their patient, a dull ache and disability progressed for over seven months. There was no history of trauma. The knee was enlarged and there was thickening of periarticular tissues. There was moderate increase of local heat, without redness of the joint. Roentgenographic examination showed thickening of soft tissues and moderate atrophy of bone. Aspiration yielded thick purulent material negative on culture. At operation the synovial cavity resembled a large abscess filled with thick gray pus, grossly resembling advanced tuberculosis, while microscopically the synovial membrane was found to be transformed into a mass of granulation tissue infiltrated with giant cells and macrophages. Many of the phagocytic cells contained the Histoplasma, some of them in enormous numbers.

Another fungus disease with articular involvement is *Madura foot.* Although this chronic inflammatory disease usually attacks the foot, it may involve the knee, thigh, buttock and rarely, the hand. Characteristically, there is marked swelling or deformity of the part with progressive disintegration of all the tissues, including the bones and joints, and granulomatous nodules on the surface with sinus openings.

Other fungus diseases such as *sporotrichosis* and *actinomycosis* may attack muscles, bones or joints with their chronic inflammatory lesions.

Among the helminth infections, *filariasis* in the stage of invasion is not infrequently accompanied by synovitis. An arthritis or a synovitis may develop in the knee or hip, occasionally with purulent effusion. In some instances fibrous ankylosis has been reported following filarial infection.

Transient swellings about joints have been noticed at times as the first symptoms of *loiasis.* In some cases, these swellings are painless; in others there is aching or burning together with swelling in a hand, arm, wrist or ankle.

Acute arthritis has been described in *onchocerciasis* with micro-filaria in the joint fluid in some patients. It is more common, however, to find small or large subcutaneous tumors in proximity to joints, especially around the knee and in the popliteal space or over the trochanters, about the elbow or about the vertebral column. The swellings may be as large as a pigeon's egg and may be painful in the incipient stage. In some cases pain is present and fistulae form, with the nodule acting as a purulent focus. Loss of function may result. Scarring frequently occurs, especially about the trochanters.

In countries in which *guinea worm* infection is endemic, this diagnosis is always suggested when a bullous blister or a sinus appears on the foot or leg. Such sinuses may be single or multiple. If the worm is near a joint, that region may become red, swollen and painful and walking may be difficult. Arthritis and synovitis frequently develop with a serous or purulent joint effusion, usually sterile. There may be fibrotic changes and contraction of a tendon such as the tendo Achilles or the hamstrings, or bony ankylosis may occur. Permanent deformity may result from secondary bacterial infection, particularly when rest in bed has been prolonged. The joint changes are induced by invasion of the joint by the guinea worm itself or merely by the nearby presence of a calcified worm. In some cases, the live worm burrows deep between fascial planes producing pains in the vicinity of joints without actual joint involvement.

Other helminth infections which may be accompanied by generalized body pain include *schistosomiasis, cysticercosis* and *trichiniasis.* In the latter disease mild or severe muscular pains occur particularly at the beginning of the period of larval migration into the muscles.

Protozoal diseases which may be associated with generalized aches and pains and discomfort in the vicinity of joints include malaria and trypanosomiasis. Severe headache and pains in the back and about the joints are commonly experienced during the high fever which accompanies a *malarial* attack. Muscular soreness may also be a symptom. Even during the premonitory stage of the disease and in chronic more or less afebrile cases, rheumatic pains frequently occur. Blackwater fever is often accompanied by severe lumbar pain.

Neuralgic pains, especially near the joints, are frequently seen in the early stages of *trypanosomiasis* (African sleeping sickness). Some patients may develop painful swelling of the feet and hands or of joints elsewhere. This may disappear after a few days to reappear at another site. Deep hyperesthesia with severe pain following slight trauma may be present especially over bony prominences (the so-called Kerandel's sign). Pains and cramps may be present in the late stages also.

Among the spirochetal diseases, those which have joint manifestations as part of their symptomatology include bejel, yaws, relapsing fever, infectious jaundice (or Weil's disease) and rat bite fever. In *bejel,* the nonvenereal treponematosis of the Euphrates Valley, the causative organism is indistinguishable from *Treponema pallidum.* This disease often shows bone changes: periosteal or endosteal proliferation with or without areas of rarefaction, or in some cases lesions resembling gummata and involving the medulla. These last may extend to the end of the bone and into the joint, pròducing localized destruction of the articular cartilage of one surface of the joint. Proliferative changes may develop about the areas of bony destruction.

The treponema (*T. pertenue*) responsible for *yaws* is another organism indistinguishable from the causative agent of syphilis. Joint pain may occur

at any stage of the disease in yaws. During the incubation period rheumatic-like pains, worse at night, may be noticed in the joints or in long bones. In the secondary stage, pains in bones, joints and muscles not infrequently accompany the irregular fever and headache. In the late stage of yaws, bones and joints may be affected in a fashion similar to that of syphilis. In some cases, one may find hydrarthrosis, in others a chronic infiltration of the synovial or perisynovial tissues, tenosynovitis or chondrosynovitis. Occasionally an entire joint may become disorganized. Ankylosis may occur and may render useless a finger, hand, large joint or whole extremity. Another feature of yaws, typical though rather infrequently seen, is the bow contraction of the little finger or less commonly of the fourth finger found in the late stage of the disease. The primary change, viz., contraction of the skin, is followed by shrinkage of the joint capsule and the deformity described.

Subcutaneous nodules are often present in yaws, most commonly on the ankle or leg. They may soften and lead to lesions of bone and deformities with deep ulceration and scarring, particularly where the bone is close to the skin. Joints may be affected secondarily from these nodules. One may also find juxta-articular nodes symmetrically placed in relation to joints, e.g., over the olecranon or over the lower ends of the femora. These nodes are movable at first, later becoming fixed.

Bone and joint sequelae may occur in as many as 20 per cent of patients with yaws with severe pain often an outstanding feature.

In *relapsing fever,* severe pains may constitute the most prominent symptom at the onset, persist throughout the course of the fever and recur when the fever recurs. They closely resemble the pains of dengue and may be present in the back, neck and loin and in the muscles, bones or joints of the limbs. In most instances, there is no real inflammation of the joint, though arthritis has been noted in some epidemics and polyarthritis has been reported as a complication in convalescence.

Muscle and joint pain is frequently present in *Weil's disease* (leptospiral or infectious jaundice). Agonizing pain in the back and limbs, particularly in the calves, perhaps with great tenderness, often marks the sudden onset of the disease and should suggest the diagnosis.

Rat-bite fever in the form due to *Spirillum minus* is called sodoku by the Japanese. It may give severe joint pains but true arthritis is uncommon. Bloch and Baldock [1] have reported a patient with pain in both knees and in the left ankle during the course of the disease. The case was diagnosed by finding *Spirillum minus* by mouse inoculation. Though uncommon in the naturally occurring disease, arthritis of the elbows and ankles has been frequently noted in artificially induced rat-bite fever.

Infections due to *Haverhillia multiformis,* the other variety of rat-bite fever, characteristically have a septicemia with metastatic arthritis along with morbilliform and petechial cutaneous eruptions.

Pains in the muscles occur also in certain other spirochetal diseases in the tropics, notably *seven day fever* and the *pseudo-dengue of Java*. In the latter pains in the legs are particularly prominent.

Among the rickettsial diseases, typhus, Rocky Mountain spotted fever, tsutsugamushi and Q fever have pains as part of their symptomatology. *Typhus fever* at its onset frequently gives pain in the limbs, especially in the calves, along with severe pain in the back and headache. These pains may be excruciating and may continue throughout the course of the disease. Such pains have on occasion led to an erroneous diagnosis of rheumatic fever. There is usually, however, no swelling or redness of the joints in typhus fever though an occasional joint effusion is encountered. Pains in the feet and legs are very common during convalescence from this disease. Similar symptoms are usually present in *Rocky Mountain spotted fever* and in *tsutsugamushi*. Pains in the back of the legs may also occur in *Q fever*.

In *trench fever* severe pains in the shin bones, particularly at night, are the classical manifestations. In some cases, even the weight of the bed clothes cannot be tolerated because of marked hyperesthesia. Joint pains are common particularly in the ankles and knees; in the chronic stages pain in the lumbar region is likely to be persistent. A distinguishing feature of all of these pains is the fact that they are uninfluenced by active or passive motion.

Joint pains are common in the chronic mild type of *Oroya fever* while a sudden onset with severe joint pain particularly in the knees, ankles and wrists, often marks the onset of the *Verruga peruviana* stage of the disease.

Among the tropical diseases caused by bacteria, joint manifestations are common in several, especially in bacillary dysentery and leprosy. Tularemia and undulant fever may also show joint involvement but need not be discussed as tropical diseases. Plague and cholera exhibit painful phenomena in the course of disease. In *bacillary dysentery* arthritis occurs in a variable percentage of patients, from 0 to 16 per cent in different epidemics. It is more common in Shiga infections than in others. The joint involvement occurs most frequently from one to three weeks after the onset of the dysentery but has been known to appear months later, occasionally after all symptoms of a previous mild dysentery have been forgotten. Single or multiple joints may be affected. One or both knees may be involved. Next to the knees, the ankles are most susceptible to attack. Dysenteric arthritis may persist four to six weeks but in the end complete recovery and return of function are to be expected. Suppuration with resultant ankylosis has occasionally been encountered, but is rare. The joint effusion in bacillary dysentery is usually straw colored and is slightly viscid. As a rule the joint fluid is sterile, though occasionally Shigella organisms are cultivated, and agglutinins are sometimes present in higher titer in the joint fluid than in the blood itself.

In contrast to its frequent occurrence in bacillary dysentery, arthritis is seldom, if ever, found in patients with amebic dysentery.

Severe generalized pain in the limbs and back commonly accompanies the onset of *leprosy*. Soon after, painful swelling of the hands and feet may appear. Later, contractures are common, as in the hand, with the resulting main-en-griffe. Excruciating pain in the toes, especially the big toes, may be present. Trophic disorders of bones and joints may develop with or without ulcerations and rarefaction and absorption may take place with gradual disappearance of bones and joints, especially in the phalanges of the hands and feet. With certain joints, especially the wrists and ankles, one occasionally sees an actual neuropathic process akin to a Charcot joint, with disorganization of cartilage and bone.

In *cholera* muscular pains in the limbs due to loss of fluid and electrolytes come on acutely and disappear rapidly with replacement therapy.

Pains in the back and limbs may occur in the prodromal stage of *bubonic plague*. If the plague bubo forms in the groin, as is usual, the leg may be held in flexion to avoid pain. With the bubo in the axilla, the arm is likely to be held in abduction. Careful examination differentiates this from actual joint pain.

Other tropical diseases of uncertain etiology may attack joints or produce pain simulating arthritis. In *ainhum*, a circular groove appears at the base of one or both little toes, less often the fourth toes. This groove gradually deepens and within a few years, as a rule, proceeds to the severance of the toe, usually without pain or ulceration. The bone beneath the constricting band has become rarefied and then absorbed.

Tropical ulcer is likely to occur on the lower portion of the foot or leg. When on the dorsum of a toe, the ulcer sometimes burrows downward to involve tendons or a joint cavity.

Pains in the back together with weakness of the legs are frequent signs at the onset of *lathyrism*, a disease not infrequent in India, Africa and other tropical countries. Spastic paralysis with ataxia are the prominent symptoms of this disease, whose etiology is thought to be the consumption in large amounts of products made of the chick-pea or a contaminating weed.

The etiology of *pyomyositis* is unknown. The disease is found particularly on the African gold coast and usually attacks the gluteal or quadriceps muscles. It may be mistaken for septic arthritis or cellulitis.

On occasions, various drugs used to treat tropical diseases may be the cause of pain in muscles or joints. Muscle cramps may occur in *aspidium* poisoning. Generalized body pains have followed the use of certain drugs employed in treating African trypanosomiasis, namely *antrypol* (the English equivalent of Bayer 205) and *tryparsamide*. Muscle stiffness may follow the intravenous injection of *antimony* preparations used for treatment of oriental sore or kala azar. Toward the end of the course of therapy, an injection may be followed after several hours by severe pains in muscles and joints along with cramps in the calves.

In addition to the joint manifestations of tropical disease, one may find all the more usual forms of joint disease in the tropics. Their prevalence

in temperate and in tropical regions differs somewhat, however. In the tropics, both rheumatoid arthritis and rheumatic fever are relatively uncommon, though they may occur with their usual frequency among European residents in many tropical areas. Some experienced workers in Central Africa, South China, India and Malaya report never having seen rheumatic fever or endocarditis in a lifelong experience in those countries. By contrast, one finds tuberculosis of the joints to be extremely common in the tropics probably because these regions have been largely unsanitated and the incidence of tuberculous infection in general is very high there. Gonorrheal arthritis has also been reported commonly in China, India and Ceylon.

Summary and Conclusions

From the standpoint of involvement of joints, tropical diseases fall into three groups: (1) diseases in which arthritis is a well-known and comparatively common complication; (2) diseases in which arthritis occurs occasionally or incidentally, perhaps as an extension from more characteristic lesions elsewhere; (3) diseases in which arthralgias and myalgias occur without definite joint involvement. (In many of these arthritis is simulated.)

Knowledge of the occurrence and course of arthritis in association with tropical diseases should contribute to accurate diagnosis of the disease and to proper assessment of prognosis for the complication.

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LIPOID PNEUMONIA IN ADULTS *

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That the problem of lipoid pneumonia is not one primarily of infants and children is indicated by the marked increase in the number of cases reported in adults in the past five years,[1] which now equal in number those observed in infants.[2, 3] In 264 cases compiled from 1927 through 1942, Sweeney [3] found 133 in infants and children and 131 in adults. Hence, the condition is not as uncommon in adults as previously thought. Of these, only 44 could be definitely ascribed to the use of intranasal mineral oil. The use of mineral oil as a laxative accounted for nearly half of the adult cases, whereas vitamin oils were the outstanding causes in children and infants, accounting for over one-third of the cases.

As Ikeda [4] has pointed out, the term *lipoid pneumonia* should be strictly confined to a productive inflammation of the lung in which the fundamental histologic alterations are directly attributable to the presence of foreign oil or fat. A few oil-laden macrophages and oil globules due to agonal or terminal aspiration in acute exudative or septic pneumonia, he pointed out, are not the criteria of this condition. The etiologic factors in adults and older children are often such that the cases may well be considered in a separate group. Ikeda has applied the term *paraffinoma* to these pulmonary infiltrations, which often simulate carcinoma of the lung in radiologic appearance. Houck [5] has followed a similar trend, and Saenz [6] also has considered the classification into adult and infantile types as important. Hence, a classification into adult and infantile types has been well established. The great variations in the clinical picture of this disease in adults and the greater variety of diseases seen in the chest as age advances make it a difficult diagnostic problem in the adult group.

Our concern in this report is exclusively with those clinical pictures occurring in adults. Since some of the types termed infantile occur in adults, our discussion concerns symptom complexes regarded as infantile [4] as well as those considered essentially adult in type. Both so-called infantile and adult types may occur in either adults or infants,[7] and the pathogenesis is fundamentally the same.

Clinically, the expressions of lipoid pneumonia may be grouped as follows:

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I. *Asymptomatic*

A. Not recognized before autopsy.
B. Physical findings leading at times to a roentgenologic diagnosis.
C. Findings on roentgenologic examination without remarkable physical findings.

II. *Symptomatic,* with the findings in *B* and *C,* above, expressed as

A. Acute pneumonitis simulating aspiration pneumonia; protracted bronchopneumonia.
B. Recurrent acute pulmonary infection with clinical evidences of repeated attacks of bronchopneumonia.
C. Low-grade bronchial or pulmonary infection which leads to roentgenologic findings.
D. Picture simulating carcinoma of the lung, with cough, pain in chest, and related symptoms leading to roentgenologic findings which simulate those of carcinoma.
E. Lipoid pneumonia incidentally found in association with other pulmonary disease.
F. Association of any of the above pictures with a clinical state predisposing to aspiration, such as bulbar palsy, multiple sclerosis, other causes of dysphagia, and severe debilitating disease.

The predominant occurrence of the asymptomatic group is well shown by reports in the literature. About one-half the autopsied series of Freiman, Engelberg and Merrit [1] was asymptomatic. The frequency of the asymptomatic group makes it difficult to determine the actual incidence of lipoid pneumonia. As Cannon [8] pointed out, most of the cases reported have been diagnosed at necropsy. The incidence probably varies widely geographically for the reported incidence of lipoid pneumonia at autopsy varies widely; for example, six in 290 consecutive autopsies,[9] seven in 101 consecutive autopsies,[10] 41 in 3,500 consecutive autopsies [1] in adults, and 39 in 2,000, 27 of which were adults.[8]

The frequency of the asymptomatic group in one autopsy series [1] was approximately 25 per cent. Of 41 cases, 10 showed no symptoms or signs. In four of these roentgenograms were taken which were negative. These fall in Group I–A of the classification given. Of this group of 41 cases, there were 10 with no known pulmonary symptoms but with either physical signs, roentgenologic evidence, or both. These constitute examples of Groups I–B and I–C of the clinical classification. The accidental finding of roentgenologic evidence of pulmonary infiltration, when chest plates are taken in periodic examinations or evaluations without regard to symptoms, produces these clinical groups.

The roentgenologic findings vary widely depending on, among other factors, the type of oil, the mode of aspiration, the "dose," and the extent of the process. We have already mentioned cases in which roentgenologic findings

were reported as normal, or within the range of normal variation of pulmonary shadows, when postmortem examination revealed the presence of lipoid pneumonia. In many instances exaggeration of the bronchovascular markings in the lower lobes may be the only evidence. Small areas of increased density may appear along the bronchial markings. Evidence of fibrous and atelectatic areas may develop in the surrounding parenchyma. This comes about apparently from the mononuclear cellular reaction to the oil in the alveolar spaces. These cells pass to the lymphatics causing engorgement, nodulation, and beginning fibrosis. Nodulation may appear and when lesions reach sufficient size areas interpreted as consolidation are seen. These areas are often more sharply defined than those of bronchopneumonia and are often not limited by the usual anatomic subdivisions of the lung.[11] The areas of nodulation are frequently very sharply defined, giving the appearance seen in bronchogenic carcinoma. This will be discussed further below. At times they may be feathery. Again they favor the bases, especially the right base, and tend to spread from the hilar areas. The upper lobes may be involved but if they are, only rarely are the lower lobes free. Hence, the picture varies from one of delicate or heavy linear markings to nodulation and consolidation. Without secondary bacterial infection in the lungs, the shadows do not change in size greatly from month to month. They may increase in size slowly. The fibrous changes may cause contractions of shadows seen in the more acute stages as time goes on. Superimposed secondary infection may cause the shadows to vary from time to time. Compensatory emphysema occurs.

It can readily be seen from these descriptions how easily confusion may occur with bronchiectasis, tuberculosis, primary and secondary malignancy, pulmonary infarction, acute bronchopneumonia, unresolved pneumonia, fungus infections and pneumonoconiosis. Obviously there is no roentgenologic picture which, by itself, is diagnostic of lipoid pneumonia.

The symptomatic group contains clinical pictures simulating nearly all types of pulmonary disease. It may be felt that no classification is necessary beyond the statement that lipoid pneumonia may simulate various pulmonary diseases of other types. However, several of the pictures are outstanding and deserve emphasis. Also, stress on the similarity of lipoid pneumonia to some other pulmonary diseases is absolutely necessary to increase awareness of its possible occurrence in specific instances. Both of these facts justify the classification.

Of the six clinical types listed in the symptomatic group, that with most dramatic symptoms is Group II–A, in which acute pneumonitis, often diagnosed as acute bronchopneumonia, is found and may run a protracted course. As a matter of fact, in bronchopneumonia which does run a protracted course oil aspiration should be suspected as the cause. The type of oil may determine the symptomatology. Animal oils, especially cod liver oil, are highly irritating, whereas some vegetable oils, olive, cotton seed, sesame, and poppy seed, are relatively nontoxic. Of the common oils producing

lipoid pneumonia cod liver oil is more likely to give an acute picture of this type than is mineral oil, which is likely to produce a more chronic reaction. This has been found true experimentally in rabbits [12] where lipoid pneumonia resulting from cod liver oil produces a more intense acute inflammation in the early stages. Acute fatal disease of short duration has also been produced in cats.[13] There are a number of clinical cases of this type reported in the literature. The first two adults [14, 15] described as having lipoid pneumonia were similar in type to these. Both died with bronchopneumonia; both had lesions interfering with swallowing.

Without a history of aspiration or the knowledge that an oil has been instilled into the chest, there would be little reason to suspect oil as the etiologic agent in bronchopneumonia. It might be found in the sputum incidentally in a search for a bacterial cause of the disease or if looked for deliberately when the cause is suspected. Usually the lesions of lipoid pneumonia are not so extensive that the patient dies of asphyxia. In our case 1 very extensive lesions without asphyxia were noted. Superimposed infection may add sufficient strain to produce asphyxia.

Another group of pneumonias closely related to this class is the aspiration pneumonia resulting from the intake of kerosene, gasoline and other hydrocarbons [16] related to mineral oil.

One of the most interesting and striking of the clinical expressions of lipoid pneumonia is that considered in Group II–B. This is the picture of recurrent pulmonary infection with clinical evidences of repeated attacks of bronchopneumonia, well exemplified in our case 1.

Case Reports

Case 1. J. E. B., 49-year old white male, was admitted to the hospital on August 12, 1944, complaining of shortness of breath, cough and weakness. The patient stated that his trouble began when he was 13 years old. He had had rhinitis and bronchitis at that time and had never been well since. Chronic cough had been present for the preceding 20 years. In the previous six or seven years he had had frank hemoptysis on two occasions and blood-streaked or rusty sputum numerous times since 1937. During the previous few months he had noticed progressive weakness, fatigue, dyspnea on exertion, cough and considerable expectoration of mucoid, purulent, blood-tinged, rusty or frankly bloody sputum. There was more expectoration in early morning and less trouble in dry, warm weather. He had been in numerous hospitals and clinics during the previous several years for his "lung trouble." In 1934 he was told that he had bronchiectasis. At various times tuberculosis, Boeck's sarcoid, fungus diseases and various other chronic pulmonary diseases had been considered but never proved. In November, 1941, a diagnosis of osteochondroplasia plastica was made by bronchoscopic examination. At the same time a specimen of sputum stained with Sudan III revealed the presence of fat. Questioning as to medication revealed that he had been taking "agar oil" (agar-agar and mineral oil) daily as a laxative from 1927 to 1939. He had also used an oily preparation with 2 per cent phenol (applied to the nasal mucosa with an atomizer) from 1936 to 1940.

Further historical data included mastoid operations at the ages of 18 and 19, tonsillectomy when 32, gonorrhea the same year, chancre of lip diagnosed by darkfield

examination when 36 years old. He had taken antisyphilitic therapy for 10 months but discontinued the alternating bismuth and arsenical injections because he felt weaker when under treatment.

Physical examination on admission on August 12, 1944, disclosed severe dyspnea. The patient died a few hours after admission. The temperature was 98.6° F. on admission, 102.6° F. at death. Previous examination showed a blood pressure of 110 mm. Hg systolic and 60 mm. diastolic, pulse of 88, respirations 22, temperature 99.4° F. He was a fairly well developed, poorly nourished white male, approximately 49, appearing chronically but not acutely ill. He was fairly intelligent and coöperative. Positive findings included slight injection of the pharynx, diminution of vocal resonance and breath sounds from the scapula to the lung bases bilaterally. A few basal râles were heard. There was an occasional extrasystole.

Laboratory data included a hemoglobin of 11 gm. (65 per cent), erythrocytes 3.9 million, leukocytes 7,500, polymorphonuclears 67 per cent, lymphocytes 33 per cent; sedimentation rate of 54 (uncorrected). The specific gravity of the urine was 1.021 and the urine showed an occasional leukocyte. Blood urea nitrogen was 9.1 mg. per cent; glucose, 103; serum protein 6.5 per cent; A/G 1.2/1. Kline and Kolmer reactions were negative on two occasions. Bronchoscopic examination showed multiple small osteochondromata involving the upper half of the trachea and upper portions of the right and left main stem bronchi. These were hard and the specimen removed was too small for microscopic study. Roentgenograms of the chest showed bilateral evenly distributed infiltration of midlung zones and bilateral hilar node enlargement. Sputum was negative for acid-fast bacilli four times by smear and twice by concentration.

The patient had had 11 previous admissions to the hospital, usually with bronchopneumonia superimposed on his chronic disease. These admissions were as follows:

(1) The patient was admitted February 24, 1942, discharged March 17, 1942. Low-grade fever was the only finding.

(2) The patient was admitted October 29, 1942, discharged December 7, 1942. The leukocyte count was 21,050 with polymorphonuclears 90 per cent, lymphocytes 10 per cent. The sputum was negative for pneumococcus. The temperature, 102° F. on admission, returned to normal on therapy with sulfadiazine.

(3) The patient was admitted on February 21, 1943, with a temperature of 103° F. Sulfadiazine therapy was instituted and the temperature dropped in three days. Patient was discharged on March 5, 1943.

(4) The patient was admitted on April 5, 1943. Temperature on admission was 102.6° F. and returned to normal on sulfathiazole therapy. The leukocyte count was 15,750 with polymorphonuclears 89 per cent and lymphocytes 11 per cent. The patient was discharged on April 26, 1943.

(5) The patient was admitted on July 28, 1943, with a temperature of 103° F. Sulfadiazine therapy was instituted and the temperature dropped to normal. The leukocyte count was 15,450, with polymorphonuclears 84 per cent and lymphocytes 16 per cent. Sedimentation rate was 24 (corrected). The sputum was negative for acid-fast bacilli on two examinations. The patient was discharged on August 7, 1943.

(6) The patient was admitted on October 30, 1943, and discharged on November 9, 1943. The temperature on admission was 105° F., and dropped to normal on sulfadiazine therapy. The leukocyte count was 20,000 with polymorphonuclears 89 per cent and lymphocytes 11 per cent. Sputum was negative on two occasions for acid-fast bacilli and on one occasion for fungi. Roentgenograms taken at this time were essentially the same as on all other admissions (figure 1).

(7) The patient was admitted on November 25, 1943, with a temperature of 101° F. Postural drainage was started and the temperature was down in three days. Urinalysis gave normal findings. The patient was discharged on November 30, 1943.

(8) On admission January 23, 1944, the patient's temperature was 103° F. and dropped to normal with sulfadiazine therapy. Blood culture was negative. Leukocyte count was 11,200 with polymorphonuclears 78 per cent, lymphocytes 22 per cent. The patient was discharged on January 28, 1944.

(9) The patient was admitted on February 19, 1944, discharged March 3, 1944. Temperature was 103° F. on admission and, with sulfadiazine therapy, returned to normal. Sputum examination showed oil (fat) globules.

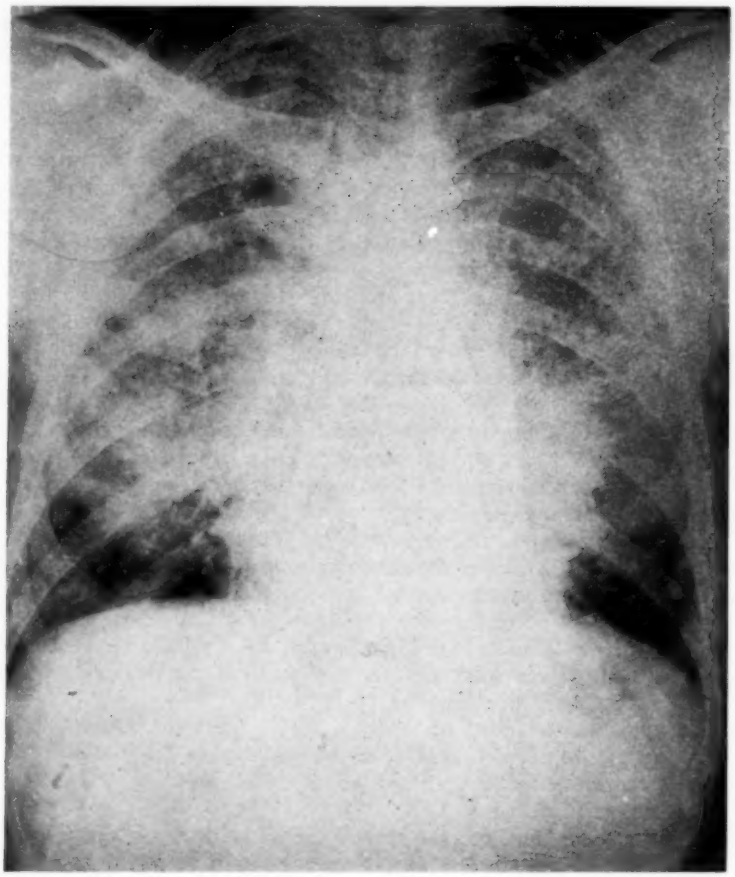

FIG. 1. Roentgenogram of the chest of Patient 1, taken on the sixth admission. It is similar to those taken at intervals from the first admission and at times when no acute infection was present.

(10) The patient was admitted on March 13, 1944, with a temperature of 102.2° F. Temperature was down in three days on sulfadiazine therapy and the patient was discharged on March 26, 1944.

(11) The patient was admitted on April 25, 1944, with a temperature of 103° F. Sulfadiazine therapy was instituted and the temperature was down in three days. Leukocyte count was 11,000 with polymorphonuclears 84 per cent, and lymphocytes 16 per cent.

Autopsy examination disclosed extensive lipoid pneumonia.

A number of examples of this type of clinical picture have been published. It appears to be the one clinical type which, by itself, should arouse suspicion of lipoid pneumonia. Still the symptomatic picture is due to infection. In our patient the pulmonary changes of the lipoid pneumonia were so extensive (figure 1) that the shadows were not markedly changed during the acute episodes. Sputum studies during these episodes may not disclose any bacterial agent to produce the picture. This was true in this patient, as well as in other reported instances of this type,[1, 17, 18] despite the fact that high leukocyte counts and clinical pictures which are generally interpreted as resulting from bacterial types of pneumonia were obtained. In each instance, except the terminal episode, our patient responded to sulfonamide therapy with return of the temperature to normal in three to five days.

Low-grade bronchial or pulmonary infection with lipoid pneumonia may simulate closely the pictures of bronchiectasis, chronic bronchitis, pulmonary tuberculosis and other types of chronic pulmonary suppuration. Moel and Taylor [19] have described patients belonging to this group. Low-grade fever or transitory slight rises in temperature, chest pain, cough, productive or non-productive, together with patches of râles and areas of dullness and bronchial breathing with all gradations of these findings down to normal, make up the clinical picture. Usually such findings are basal, often confined to the right side only. Blood-streaked sputum is uncommon, but may occur. In bronchiectasis the sputum is usually more profuse, clubbing of the fingers may be seen, and the roentgenogram with lipiodol is diagnostic. So-called "unresolved pneumonia" represents a diagnosis difficult to establish and probably oil is the cause of many of these cases. Pulmonary infiltrations may not be recognized as lipoid unless the possibility is kept in mind and a possible mechanism sought when the cause of any pulmonary infiltration is considered.

In Group II–D the picture simulating carcinoma of the lung is given. We have seen one patient who has shown this picture. The following is a summary of this case.

Case 2. E. H., a 63 year old bottle washer in a chemical factory, was admitted to the hospital on June 25, 1943, complaining of cough and weight loss. He had felt well until one week before, but had lost an indeterminate amount of weight during the previous year. He had had "bronchitis" for the previous 20 years and had coughed up about a teaspoonful of whitish sticky sputum a day. Just previous to admission pain had developed in the right lower chest anteriorly; it was aching in character, coming on usually at night if his head was not elevated or if he lay on his right side. The pain radiated across his chest toward the sternum and had no relation to meals, exercise, or emotions. It occurred during the day if he reclined on his back or right side. He had had night sweats and chilly sensations for one week prior to admission.

The patient had had a "lump" cut off his head three years previously. Casual questioning elicited no history of medication, but close questioning indicated that he had taken an ounce of mineral oil five or six nights each week for some years to avoid constipation.

Physical examination showed a somewhat thin white male, 63 years of age, who did not appear acutely ill. The blood pressure was 140 mm. Hg systolic and 80 mm. diastolic, temperature 98.8° F., pulse 84, respirations 24. The scalp and skull showed no gross abnormalities. The thyroid gland was moderately and diffusely enlarged. There was an old perforation of the left ear drum; the eyes and nose were normal. There was almost complete edentia. The tonsils were moderately enlarged and cryptic. The chest was symmetrical. The expiratory phase of respiration seemed prolonged, and expiratory wheezing râles were heard in both lung bases posteriorly. There was increased vocal fremitus at the right lung base posteriorly. The heart appeared to be normal. The liver edge was barely palpable on deep inspiration. There was a small inguinal hernia on the right side. Rectal and genital examinations revealed no gross abnormalities. The extremities were normal; the reflexes were physiologic.

Laboratory data included a hemoglobin of 70 per cent, erythrocytes 3,850,000, leukocytes 10,150 with polymorphonuclears 74 per cent, monocytes 6 per cent, and lymphocytes 20 per cent. The urine was essentially normal except for an occasional pus cell. Phenolsulfonphthalein excretion was 55 per cent at the end of two hours. Maximum urinary specific gravity was 1.023. Blood chemical determinations showed carbon dioxide combining power 66 volumes per cent, blood urea nitrogen 15.4 mg. per cent, serum protein 6.51 gm., blood chlorides 582 mg. per cent. Kline and Kolmer reactions were negative. Mantoux test was negative. Nine sputum examinations failed to reveal tubercle bacilli. Bronchoscopic examination was negative. Electrocardiogram revealed a QRS duration of 0.14 sec., and was reported to show defective intraventricular conduction with definite electrocardiographic evidence of myocardial disease. Roentgenogram of the chest revealed an area of infiltration in the midlung zone behind the anterior end of the right fourth rib (figure 2). Bronchograms were normal.

Serial roentgenograms of the chest failed to show any clearing of the infiltrative lesion in the right lung and on July 26, 1943 (approximately one month after admission) a right pneumonectomy was done because it was felt that the patient had a bronchogenic carcinoma of the right lung. The patient had an uneventful postoperative course and was discharged two weeks later. He has been able to return to work and is being followed in the clinics.

The pathologic specimen showed the characteristic changes of lipoid pneumonia with fat stains.

A number of cases of this type have been reported in the literature.[4, 20, 21, 22, 23, 24, 25] The first European case [25] showed large tumor-like shadows on which irradiation therapy was tried. The roentgen appearance of these shadows, as already described, may lead to consideration of carcinoma as a diagnosis. In our patient the findings were so typical that pneumonectomy was done and the diagnosis of lipoid pneumonia made only after study of the removed lung. Brown and Biskind also reported a case in which a surgical approach was carried out apparently because of suspected malignancy. Removal of a portion of a lobe was done. It is evident, as Brown and Biskind stated, that the possibility of lipoid pneumonia must always be considered when an unconfirmed diagnosis of a malignant pulmonary growth is entertained. History and sputum studies may be helpful. Differences in the course of the disease, especially by roentgen-ray studies, and bronchoscopy with biopsy material are important in the differentiation.

Group II–E includes pictures of lipoid pneumonia, any of which may take the characteristics of those described above, in association with other pulmonary disease. This group is separated from Group II–B in which bronchopneumonia occurs with lipoid pneumonia in that the repetition of that picture makes it such a unique and almost diagnostic picture that it warrants separate consideration. Also in the present group the association of the two

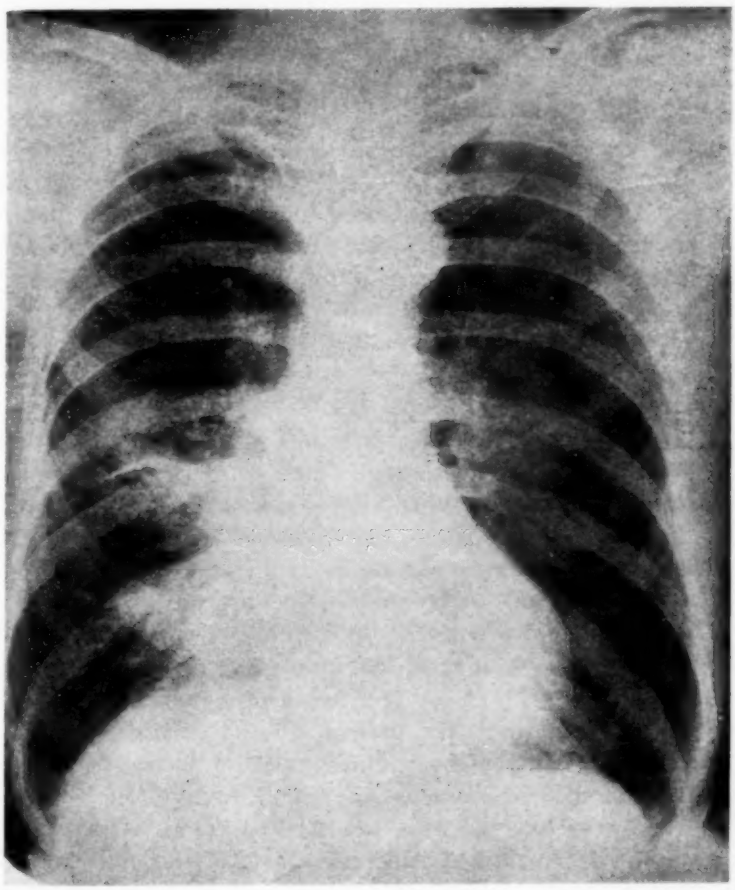

FIG. 2. Roentgenogram of the chest of Patient 2, taken on admission to the hospital, showing an area of infiltration in the midlung zone on the right side.

diseases is accidental. A good example is the case of Wood [26] in which lipoid pneumonia was found associated with so-called bilateral alveolar carcinoma of the lung. The question of the possible tumor-producing properties of mineral oil was discussed in that report.

The final group to be considered requires little discussion. Here the clinical pictures again may be those of any type discussed above, associated with extrapulmonary disease which predisposes to oil aspiration and which,

therefore, is likely to be found in association with lipoid pneumonia. The importance of such disease in the causation of lipoid pneumonia is widely recognized and is discussed below in the remarks on diagnosis. Bulbar palsy, cleft palate, convulsions and spasms, frequent gagging and vomiting, debilitating disease, difficulties in swallowing associated with esophageal diverticula,[27] cerebral birth injuries, congenital neurologic disorders, dysphagia, brain tumors, loss of cough or gag reflex, are examples. We have seen several examples of this type secondary to bulbar palsy.

Lipoid pneumonia in adults is not uncommon in the older age groups. This was not shown in our two cases, but in general the older age group predominates. The two cases do show the two chief routes of administration of the oil—the nasal and the oral. This generally results from self-administration over long periods of time. Exceptions, of course, occur at times. Whereas in infants the chief agents are cod liver and other vitamin-containing oils, milk and liquid petrolatum, in adults liquid petrolatum itself is the chief offending agent. This material cannot be metabolized by tissue enzymes whereas some of the animal and vegetable oils may be. It remains as a foreign body irritant. Inflammatory reactions with it may be due to the drug dissolved in the mineral oil.

Amounts entering the lungs depend on the dose, the frequency of application, and the effectiveness of the function of the epiglottis. Mineral oil is light and does not stimulate the cough reflex.

In adults the rôle of such predisposing factors as lesions interfering with swallowing and debilitating disease has already been discussed. Chronic infection of the upper respiratory passages may lead to the use of oily drops or sprays (sprays are more dangerous, as in our case 2), or a debilitated patient may take the oil by mouth. In infants lesions similar to those in adults, such as tracheobronchial fistula, laryngeal paralysis and esophageal disease, may contribute, but most frequently other circumstances, such as forced feeding, the administration of oily substances and attempts to feed in comatose states, are responsible. In children the pictures may be similar to some of those seen in adults, especially where mineral oil is the causative agent. Mild respiratory symptoms with a low-grade pneumonia, the repeated occurrence of superimposed infection, as described in the adult group for example, may occur. In children, too, especially if the picture is recognized early and the oil withdrawn from use, the process in the lung and the roentgenologic findings may undergo resolution.[4] In adults persistence of the picture and chronicity are the outstanding characteristics.

Even in cases in which a violent reaction occurs producing acute types of pneumonitis, as already stated, chronicity develops, for example in "non-resolving bronchopneumonia." The latter process represents a granulomatous productive inflammation which, when clearly localized, has a dense fibrous and neoplastic appearance.[4] By roentgenologic study these characteristics are brought out and malignancy may be suspected. If more widespread, tuberculosis, various types of pneumonia or bronchial disease with

secondary pneumonitis, are suspected. Periodically acute superimposed infection, recurrent pneumonia, may appear, giving a distinctive picture. Sudden or acute reactions may not appear but, after prolonged use of the oil, sometimes for years, may arise from complicating infection of various types and degrees. The condition may be found through roentgenologic study after chest findings or on routine roentgenogram without chest findings. Both may be negative and the patient go to postmortem examination with unsuspected lipoid pneumonia found at autopsy.

Although the pulmonary symptoms are said [4] to be essentially the same in all cases, differing only in degree or as the result of secondary infection, there are from patient to patient differences in the symptomatic picture, and in roentgenologic or physical evidences, which make for distinct clinical types. The emphasis of these types is the chief justification for our classification, for only by awareness of the possibility of the occurrence of lipoid pneumonia when such pictures arise will the diagnosis be made.

Clinical diagnosis rests primarily upon a strong suspicion of the disease when other explanations of the clinical picture are not well established. Physical findings are of little differential value, but are extremely important for they lead to roentgenologic investigation and diagnosis. Of Freiman, Engelberg and Merrit's 47 cases,[1] apparently only seven were diagnosed clinically. In the group collected by Bishop,[28] 23 of 136 were diagnosed during life. A glance at the classification of clinical pictures we have given indicates that most of the usual pulmonary diseases may be simulated or may be present as complicating disease. The history of the use of an oil, either as drops or by ingestion, increases the possibility that the picture results from oil aspiration. A defect in swallowing or a generally debilitating state adds to the picture sufficient evidence for a tentative diagnosis. It is usually stated that defects in deglutition and debilitated states are likely to occur as predisposing factors. However, many instances have occurred in healthy individuals without such states. This was true in our cases and is especially true with intranasal medication over long periods. One must remember that the history of the use of an oil is likely to be neglected and is often elicited only after the lipoid pneumonia is suspected.[22] Most important is the continued high suspicion of the disease in the situations already outlined. Demonstration of the lesions by roentgenograms does not settle the diagnosis, for there are no pathognomonic roentgenologic signs. Slow change in the character of lesions, with serial examinations, particularly in those located in the lower lobes, and a bronchopneumonia which fails to resolve and roentgenologic findings out of proportion to clinical symptoms and signs should lead to attempts to obtain the clinical associations described above. Confirmation may be sought by demonstration of oil in the sputum several days after oil has been discontinued as nose drops or by mouth. This may be done by letting sputum stand, then covering it with a cigarette paper to absorb the oil droplets or by microscopic search for oil. Aspiration biopsy of the lung has been advocated.[18, 29] In one instance [29] the material aspirated

by needle was allowed to settle and a layer of oil formed over the bloody material.

Conclusions

1. The known frequency of lipoid pneumonia in adults demands continued alertness for the possibility of this diagnosis when any pulmonary picture without proved cause presents itself.

2. A grouping of the clinical expressions of lipoid pneumonia in adults is given. Although lipoid pneumonia may simulate nearly all types of pulmonary disease a classification of the clinical expressions is necessary because several of the pictures are outstanding and deserve emphasis. Also stress on the similarity of lipoid pneumonia to some other pulmonary diseases is absolutely necessary to bring this possibility to mind in specific instances.

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THE RECOGNITION AND CLINICAL SIGNIFICANCE OF AURICULAR HEART SOUNDS *

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THE diagnosis of cardiac disease is a clinical problem. Observation and evaluation of the sounds accompanying cardiac activity are of great importance. The electrocardiogram is of value in the analysis of arrhythmias, and is often useful in confirming a clinical diagnosis of myocardial injury. As Levine so aptly stated: "It is a general axiom that the more thoroughly one understands electrocardiography the less one needs it." [1] Auscultation of the heart remains a most valuable clinical procedure, not only in the recognition of valvular heart disease, but in identifying arrhythmias as well.

The problem of the systolic murmur is a generally recognized one. That a systolic murmur may be present without anatomically demonstrable cardiac abnormality is a common observation. Many are hesitant to regard a systolic murmur as significant in the absence of other findings, such as a diastolic murmur, cardiac enlargement or other evidence of cardiac disease. More recently there has been a willingness to regard as pathological systolic murmurs with certain characteristics such as accompanying thrill, harsh quality, wide transmission, long duration or loud intensity.

As a corollary to the skepticism in some quarters concerning the significance of systolic murmurs, many are prone to accept the diastolic murmur per se as evidence of cardiac disease. It is often difficult to differentiate between presystolic "murmurs" and presystolic "sounds"; and between a split first heart sound and a first heart sound preceded by an auricular sound. Misinterpretation may lead to a mistaken diagnosis of heart disease. This paper is an effort to aid in the clarification of such problems.

The physiological and pathological variations of the sounds resulting from or accompanying activity of the auricle, and an attempted explanation of the mechanism involved comprise the subject matter of this discussion.

On auscultation of the normal heart one does not commonly distinguish any separate sound accompanying auricular activity. Auricular sounds are usually faint, low-pitched, dull and of short duration, and are easily obscured by the normal first heart sound which closely follows it, since the latter is louder, higher-pitched and sharper. However, when auricular contraction occurs well in advance of ventricular systole, certain diastolic sounds may be audible.

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The stethographic records upon which this paper is based are from the Department of Medicine, Johns Hopkins Hospital.

This is best demonstrated in cases of A-V dissociation, in which, with the auricles contracting independently of the ventricles, a low-pitched sound may be heard during diastole. When recorded stethographically, these sounds occur at the peak of the a-wave of the jugular pulse, and about 0.18 second after the beginning of the P-wave of the electrocardiogram. This relationship to the electrocardiographic and pulse signs of auricular activity would indicate that these sounds are associated with such activity. In lesser degrees of heart block a sound produced by auricular activity may be noted in some patients.

That the auricular sound actually consists of two parts was stated by Sir Thomas Lewis in 1914,[2] and demonstrated stethographically by Cossio and Fongi in 1936.[3] The first part of the auricular sound was recorded during the height of auricular systole, and was recorded best by a microphone placed in the esophagus, which is in contact with the auricular wall. This sound is produced, they believe, when the blood contained in the auricles is compressed by the tense auricular walls, and results from the vibration of the auricular walls and of the compressed blood. This first part of the auricular sound is transmitted to the precordium more easily in children than in adults, in whom it is usually not heard. In children it may be heard apart from the first heart sound, especially when the auricles are contracting more actively under the influence of exercise or emotion.

The second part of the auricular sound appears *after* the height of auricular activity, and is due to the vibration of the auriculoventricular valves and to the tension of the ventricular wall. This second part results from vibrations set up by the blood ejected by the auricle, and, therefore, does not appear until auricular systole is well advanced. The second part of the auricular sound is best heard from the precordium because of its origin from the ventricles in close contact with the chest wall, and usually blends with the sounds accompanying ventricular contraction to form the normal first heart sound. It is this second part of the auricular sound which is heard in some cases of heart block, where the prolonged interval between auricular and ventricular systole prohibits such blending of auricular and ventricular elements of the first heart sound. This failure of fusion results in a sharper first heart sound as well.

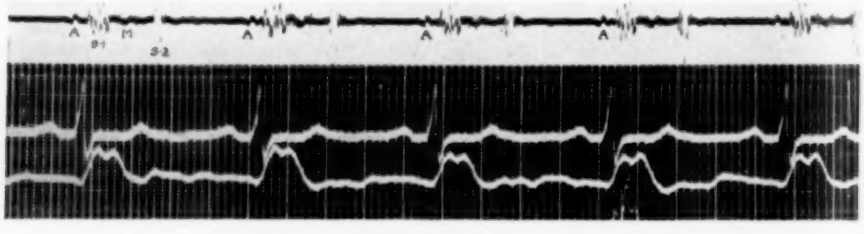
Auricular sounds may be recognized not only in patients with cardiac arrhythmia, but in patients with normal cardiac rhythm also. In children with active normal hearts the first part of the auricular sound may be audible, as mentioned above. Auricular sounds have been noted clinically and recorded stethographically in patients with hypertension (figure 1), sickle cell anemia, and Besnier-Boeck-Schaumann disease in the absence of valvular deformity or cardiac failure. A loud presystolic sound simulating that of mitral stenosis may be heard in some patients with hyperthyroidism.

A first heart sound preceded by an auricular sound must be differentiated from a split first heart sound. Usually both components of the so-called split first sound are fairly high-pitched and of almost equal intensity and

duration, and are recorded after the beginning of the QRS complex of the electrocardiogram. If the double sound at the beginning of the cardiac cycle consists of an auricular sound preceding the first sound, the auricular component is softer and lower-pitched than the ventricular component which follows it, and is recorded before the beginning of the QRS complex.

Very striking is the occasional finding of a late diastolic crescendo murmur in patients with syphilitic aortic insufficiency. Described in 1862 by Austin Flint,[4] this murmur, unlike the presystolic murmur of mitral stenosis, may be high-pitched and may be louder and of longer duration at the pulmonic area than at the apex. A single loud auricular sound such as occurs in patients with cardiac enlargement or failure should not be called a Flint

APEX



AURICULAR SOUNDS: HYPERTENSION

FIG. 1. The upper record is the stethogram of the heart sounds at the apex. The middle record is the electrocardiogram Lead II, and the lower record is the jugular pulse.

A: Auricular sounds
S–1: First heart sound
M: Systolic murmur
S–2: Second heart sound

It will be noted that the second sound is of greater intensity than the first sound at the apex in this patient with hypertension. The auricular sound is low-pitched and is recorded before the QRS complex of the electrocardiogram.

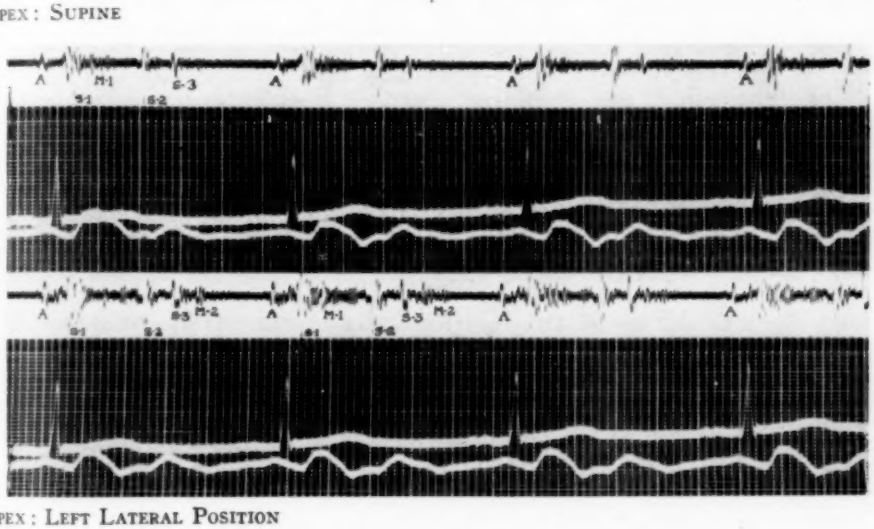
murmur. The Flint murmur is caused by a functional mitral stenosis: blood regurgitates through a damaged aortic valve, striking the anterior mitral curtain and pushing it into the blood stream passing from auricle to ventricle, thus producing a functional mitral stenosis, inasmuch as blood expelled during auricular contraction must force a channel through the approximated valve leaflets, resulting in the production of an audible presystolic murmur.

Gouley [5] described a characteristic deformity of the right aortic leaflet found at autopsy in 10 patients with an Austin Flint murmur: a groove directing the blood to the anterior mitral curtain.

Presystolic murmurs are most commonly encountered in rheumatic mitral stenosis, although as just demonstrated, auricular sounds and presystolic murmurs may be heard in the absence of such valvular involvement. There are some patients with mitral stenosis proved at autopsy in whom a systolic murmur had been the only abnormal sound noted, but who did present other evidence of cardiac disease. In mitral stenosis the first sound

may be accentuated owing to summation of the initial vibrations of the normal first sound with the terminal vibrations of the auricular sound. After a long diastole the mitral valve leaflets may be almost floated back into position before ventricular contraction, producing, therefore, a first sound of diminished intensity.

That the presystolic murmur of mitral stenosis is dependent upon effective auricular contraction is demonstrated by its absence in auricular fibrillation and its presence in patients with mitral stenosis and A–V dissociation.



Auricular Sounds: Effect of Position

Fig. 2. In each of the above records the upper tracing is that of the stethogram at the apex, the middle tracing is the electrocardiogram Lead II, and the lower tracing is the jugular pulse.

A: Auricular sound
S–1: The first heart sound
M–1: Systolic murmur
S–2: The second heart sound
S–3: The third heart sound
M–2: The mid-diastolic murmur of mitral stenosis.

It will be noted that the record of the heart sounds with the patient in the left lateral position brings out the mid-diastolic murmur of mitral stenosis which follows the third heart sound. The auricular sound is also louder in this position, and is more easily seen to be followed by a presystolic murmur. It will also be noted that the third heart sound (S–3) is recorded at the apex of the v-wave of the venous pulse, indicating the time of opening of the mitral valve.

In the latter case a low-pitched rough murmur may be noted when the auricle contracts during ventricular diastole. In the former case the only auscultatory sign of mitral stenosis may be the mid-diastolic apical murmur produced by the rapid ventricular inflow through the stenotic valve early in diastole. During tachycardia with auricular fibrillation, however, there may be a crescendo character to the terminal part of the mitral diastolic murmur. This is caused by a summation of the mid-diastolic murmur and the normal

first sound due to the shortening of diastole, and not by auricular contraction which normally occurs late in diastole.

In mitral stenosis with normal sinus rhythm one may at times hear a mid-diastolic apical murmur and an accentuated auricular sound. Occasionally these may be present during acute rheumatic fever and disappear after the acute episode has subsided. A single auricular sound noted with the patient supine may, in the left lateral position, become louder with a presystolic murmur now following it (figure 2). Exercise may cause a presystolic murmur to be more easily heard. At times such accentuation results from the tachycardia and shortened diastole, with summation of the mid-diastolic and presystolic murmurs.

The intensity of the presystolic murmur depends upon the rate of blood flow through the mitral valve, and varies in different cycles. When the auricle contracts early in diastole with the ventricle empty the murmur is louder; it may be absent after long diastoles because of the inability of the auricle to inject blood into an already filled ventricle.

The principles demonstrated in rheumatic mitral stenosis may be applied to auricular sounds in other conditions. In an active normal heart the rapid blood flow may fill the ventricle early in diastole; contraction of the auricle completes this filling and closes the mitral valve before ventricular systole, producing an audible presystolic sound. In cardiac failure the incompletely emptied ventricle may be filled early in diastole as a result of the increased intra-auricular pressure. If this serves to approximate the valve leaflets and distend the ventricular walls early in diastole a protodiastolic gallop may result. Systole of the dilated auricle later in diastole may produce a presystolic gallop sound.

This paper is not an exhaustive survey of the sounds resulting from auricular activity, but rather calls attention to sounds which frequently are overlooked or misinterpreted, emphasizes the importance of their clinical recognition, and presents theories concerning the mechanism of their production.

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CASE REPORTS

MEDITERRANEAN TARGET-OVAL CELL SYNDROME IN AN ADULT CHINESE MALE: REPORT OF A CASE*

By I. J. Greenblatt, Capt., Sn.C., A.U.S., T. D. Cohn, Maj., M.C., A.U.S., and H. L. Deutsch, Capt., M.C., A.U.S.

In an extensive report on Mediterranean target-oval cell syndrome, Dameshek [1] proposed the following criteria for its recognition: (*a*) "The racial factor, (*b*) a reduction in hemoglobin concentration in association with a low color index, (*c*) refractoriness to iron therapy, (*d*) the presence of increased numbers of target cells and reticulocytes, usually in association with oval and stippled red blood corpuscles, (*e*) the presence of increased hypotonic resistance of the erythrocytes and (*f*) the absence of such conditions as hepatic disease, steatorrhea, bleeding or lead poisoning." He suggested a probable relationship between this syndrome and Cooley's anemia. It is well known that Cooley's anemia and Mediterranean target-oval cell syndrome are limited almost exclusively to those peoples who reside or whose ancestry stems from the Mediterranean area. However, an authenticated case of Cooley's anemia was reported by Foster [2] in a six and one half year old Chinese female whose mother had a "low grade erythroblastic anemia."

The following is the report of a case of Mediterranean target-oval cell syndrome occurring in a soldier of pure Chinese ancestry who was born in China and came to this country at the age of 15 years.

Case Report

Private L. Y., a 29 year old Chinese male, was admitted to the hospital complaining of a feeling of persistent pressure in the epigastrium for two days. He vomited three times during this period. There were no other complaints except for a feeling of weakness for as long as he could remember.

Past History. He discovered that he had syphilis in 1937 and had received specific therapy for the past three years. In the Army he received 30 injections of mapharsen and 12 of bismuth over a period of seven months. At no time was there a history of any reaction. On his present admission the Kahn reaction was negative.

Physical Examination. The patient was a fairly well nourished Chinese male who did not appear acutely ill. Examination was completely negative. Temperature, pulse and respirations were within normal limits.

The clinical impression was simple pylorospasm. He vomited once and his symptoms completely subsided at the end of 24 hours. However, the weakness persisted throughout his hospitalization.

Laboratory Data. A routine blood study revealed hemoglobin 83 per cent, red blood cells 6,300,000 per cu. mm., white blood cells 7,300 per cu. mm. with a normal differential. Color index 0.66. A Wright stained smear showed large numbers of polychromatophilic red blood corpuscles, a moderate macrocytosis and numerous red

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blood corpuscles with basophilic stippling and a moderate degree of hypochromia. Approximately 30 per cent target cells were seen. Oval cells were present in every field (figure 1). To be certain these were target cells instead of artefacts heparinized venous blood was examined under the dark-field microscope.[3]

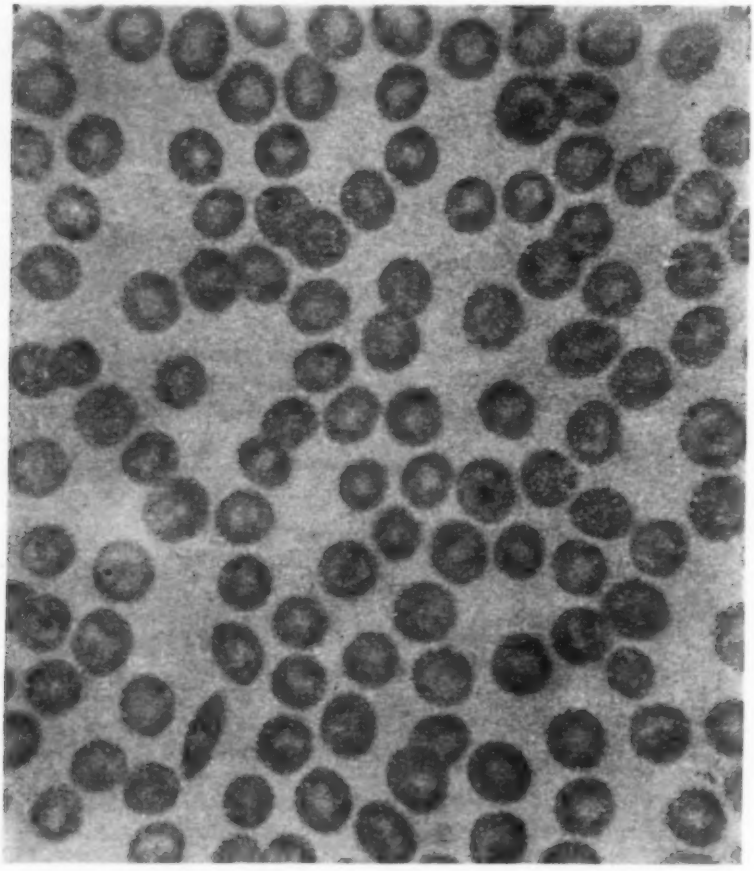

FIG. 1. Target cells and an oval cell on blood smear as seen with oil immersion.

Numerous hematological studies were made over a period of one month. The following data are average figures.

TABLE I

Hemoglobin	83% [9] *
R.B.C.	6,300,000 per cu.mm.[8]
Color index	.66 [8]
Hematocrit	.41 [3]
W.B.C.	9.0 per cu.mm.[8]
Differential	normal limits [10]
Fragility of R.B.C., Hemolysis begins at	0.42%
Fragility of R.B.C., Hemolysis complete at	0.24% [5]
Reticulocyte count	3.3% [4]
Platelets	400,000 per cu.mm.[3]
Bleeding time	1 min. 15 sec.
Coagulation time	2 min. 45 sec.

* Small numerals indicate number of tests performed.

Studies of 15 Wright stained blood smears revealed approximately one stippled red blood corpuscle, one to two oval cells, six to eight target cells and one to two polychromatophilic corpuscles per oil immersion field. There was a moderate degree of anisocytosis, poikilocytosis and hypochromia. A bone marrow smear prepared from a sternal aspiration showed a noticeable increase in erythroblastic activity with numerous oval cells, target cells and many stippled and polychromatophilic red blood corpuscles. Sickling traits were absent.

Other Laboratory Data. Urinalysis was negative for sugar and albumin with a few white blood cells per high power field in the centrifuged specimen. Serum albumin was 4.5 per cent, globulin 2.7 per cent. Sedimentation rate was 2.2 mm. per hour (Wintrobe). Urobilin plus urobilinogen excretion in the feces was 270 mg. in 24 hours and in the urine 2.33 mg. in 24 hours. Total fat in feces was 11.5 per cent. The cephalin-flocculation test was negative. The icteric index was 8. The fecal examinations were negative for occult blood. Blood lipase was 0.4 unit. Thiamine was 2.12 micrograms per 100 c.c. in the urine.[4] Examinations for lead in urine and blood were within normal limits.

Roentgenological studies of the gastrointestinal tract with special attention to the small bowel were negative. Roentgenograms of the long bones were negative. The skull as shown by roentgenogram was of the oxycephalic type.

Hospital Course. The patient remained well during his five weeks in the hospital except for his asthenia. A 15 day course of 2 grams of ferrous sulfate daily was without effect on the hemoglobin or red blood corpuscle count. A five day course with liver extract likewise had no effect on the hemoglobin, red blood cell and reticulocyte count.

Summary and Conclusions

The first recorded case of Mediterranean target-oval cell syndrome in an adult Chinese male is reported. The criteria as postulated by Dameshek [1] for this condition are fulfilled in every respect except the racial factor. To quote Cooley and Lee [5] in their discussion of erythroblastic anemia: "We are not inclined . . . to lay great stress on the limitation of this or any other similar disease to a particular race."

We wish to express our thanks to Col. Wm. S. Culpepper, M.C., Commanding officer, for his cooperation.

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PRIMARY ENDOTHELIOMA OF THE PLEURA: REPORT OF A CASE IN A PATIENT WITH CHRONIC LYMPHATIC LEUKEMIA *

By THEODORE S. EVANS, M.D., F.A.C.P., MORGAN Y. SWIRSKY, M.D., and HYMAN M. CHERNOFF, M.D., *New Haven, Connecticut*

THE etiology of leukemia at the present time is still not satisfactorily explained. Factors such as infection, trauma, drugs, toxins, and exposure to radioactive substances have been advanced as possible causes, and these have been thoroughly reviewed by Forkner.[1] More intriguing is the suggested relationship of leukemia to neoplastic diseases, and there is much evidence to support the classification of leukemias as a variety of neoplasia. This view has been championed chiefly by Babes,[2] Mallory,[3] Weber and Bode,[4] and others. Since 1878 the coexistence of the leukemias with other forms of neoplasia has been noted repeatedly by various investigators and has suggested to them an interrelationship. Both Forkner[5] and Morrison et al.[6] have summarized the accepted cases in this group. A review of material presented by these and other authors fails to disclose any previous report of the association in the same individual of chronic leukemia and primary pleural endothelioma, and it is for this reason that the following material and case report are being presented.

Although in the past some have doubted the existence of such an entity as primary endothelioma of the pleura, most modern pathologists recognize such a class of tumor growth. In 1767 Lieutaud[7] reviewed and published a study of 3000 autopsies among which he described two cases of apparent pleural endothelioma. However, in 1870 Wagner[8] first recognized this pathological entity and described it as a "tubercle-like lymphadenoma." The first two cases definitely diagnosed as endothelioma of the pleura to be reported in the American literature were presented by Beggs[9] before the New York Pathological Society in 1890. Since that time a number of cases have been reported, but the belief still persists that this is a rare type of tumor. There is no doubt that many cases of pleural endothelioma have been overlooked because there is no characteristic clinical or roentgenographic picture. The symptoms most often suggest a chronic inflammatory disease process, thereby misleading the clinician as to the underlying malignant character of the lesion. It is a slow-growing tumor and metastases usually occur late in the course of the disease, long after the initial growth has become widely distributed over the contiguous pleural surfaces. This tumor shows an age distribution common to most neoplasms, being found most frequently in individuals in the 40–60 year age group. Goeters[10] has noted this type of tumor in children, but this is a rare occurrence. Hibler[11] described such a tumor in a child of five years. It is generally believed that males are more frequently affected than females, and Birnbaum[12] claimed that it occurs twice as frequently in males as in females. Either pleural sac may be the site of the initial lesion, but Dubray and Rosson[13] stated that the right pleural sac is more commonly involved.

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From the Ward Medical Service, Grace Hospital, New Haven, Connecticut.

As stated previously pleural endotheliomata have no characteristic clinical picture. When involvement of the pleura is slight there may be few if any symptoms. The onset is usually gradual with the patient unaware of any symptoms except some exertional dyspnea, which soon may become progressive. Many other cases start as an acute pleurisy with intermittent intense pleuritic pains which gradually become constant and are accompanied by a non-productive cough, progressive weakness and some weight loss. Fever may be present, but in the majority of cases it is of no significance. Hemoptysis is usually absent. Physical examination of a patient with a fully-developed clinical picture reveals him to be dyspneic, orthopneic, and sometimes cyanotic. The temperature is usually normal, but the pulse and respiratory rates are elevated. The chest findings are those of pleural effusion with shifting of the mediastinum to the contralateral side, and roentgenogram merely confirms these findings. However, Doub and Jones [14] report that thoracentesis with air replacement of the fluid removed may reveal multiple tumor nodules on the surface of the pleura in films taken after such a procedure. Other roentgenologists feel that only thickened pleura can be seen following the production of such an artificial hydropneumothorax. Thoracentesis in itself may be of diagnostic aid. Several authors, Dubray and Rosson,[13] Rosenbaum, and Birnbaum [12] have made significant mention of the great resistance frequently encountered when the thoracentesis needle reaches the pleura and of the marked force necessary to insert the needle into the pleural cavity. The fluid in the early stages can be serous or serosanguinous, but in the usual fully-developed case it is frankly bloody. Furthermore, rapid reaccumulation of the effusion is the rule and with each tap the fluid generally becomes more bloody, so that these points, too, are of diagnostic significance. Lichtenstein [15] has pointed out that the dyspnea is slightly if at all relieved by thoracentesis and this is an important differential point from tuberculous pleurisy. The fluid resembles an inflammatory effusion, but malignant cells are often reported in the pathological examination. Saccone and Coblenz [16] do not feel that microscopic examination of the fluid is of much value, pointing out that "even clumps of cells with mitotic figures are not reliable criteria since mesothelial cells can grow and multiply in such fluids."

Once symptoms have appeared the clinical course is progressively downward with gradually increasing weakness, cachexia, and secondary anemia, symptoms all common to any advanced malignancy, plus marked dyspnea and orthopnea. Death is usually due to cardiac or respiratory failure and is often preceded by a comatose state. The duration of the illness is variable and there is no statistical agreement as to life expectancy from the onset of the first symptoms. Dubray and Rosson [13] give six to nine months as life expectancy, whereas Geschickter [17] feels that the average duration is two years. Treatment is essentially palliative, as the disease is invariably fatal.

The gross appearance of pleural endotheliomata at autopsy presents several striking features. The corresponding lung is usually completely encased and compressed by markedly thickened pleura which in some cases has measured 1 to 1.5 cm. in cross-section. In the majority of cases the greatest pleural thickening occurs at the base of the lung, especially in the diaphragmatic pleura. In the fully developed case the lung of the involved side is collapsed against the hilus and a hemothorax is present. A gristle-like sensation is obtained on transection of the abnormally thickened pleura. Inspection reveals the inner

surface of the pleura to be finely nodular in type, bearing out the impression that the process first appears as multiple nodules on the surface of the pleura which subsequently fuse. The lung parenchyma itself is usually not invaded by tumor, but frequently tumor cells do invade the septa producing nodular masses. Although metastases to the axillary and cervical lymph nodes may occur they are, nevertheless, infrequent, but metastatic involvement of the peribronchial and mediastinal nodes is a common finding. The process may also spread to the neighboring pericardium, the contralateral pleura, and through the diaphragm to the peritoneal cavity to involve the mesentery near its intestinal attachment, the appendix, liver, spleen, kidney, adrenal, and infrequently the ovaries and inguinal lymph nodes. In the case of Barrett and Elkington [18] the spleen was entirely surrounded by a layer of growth which bound it to the chest wall and diaphragm. On microscopic examination, the tumor growth consists of cells moderate in size, polyhedral or flat, with hyperchromatic vesicular nuclei and faint nucleoli. These cells may lie in small alveolar arrangement or in long single or multiple rows between cellular or hyaline connective tissue to which they are usually intimately adherent. An infrequent finding is hyaline corpora amylacea-like bodies which are said to be characteristic. According to Ewing [19] the origin of the tumor is usually referred to the cells of the subpleural lymph spaces or to the lining cells of the pleura.

Case Report

Patient A. C. C., a 40 year old married white female, was first admitted to Ward Medical Service Grace Hospital on January 12, 1944 with a chief complaint of "leukemia" of five years' duration. She stated that six years before entry (1938) she developed an exfoliative type of skin lesion with subsequent shedding of nails and much skin, but that under the care of a local dermatologist this condition gradually receded. A few months later the condition recurred and a routine blood count revealed a red blood cell count of 4.3 millions, hemoglobin of 73 per cent, and white blood cell count of 6,100 with polymorphonuclears 44 per cent, monocytes 16 per cent, and 40 per cent unidentified cells. These latter cells were large with a single nucleus presenting many of the characteristics of the monocyte, but not definitely identified as such. Physical examination at that time revealed no abnormalities except for the skin condition. A biopsy of the skin revealed the following findings: "The epithelium is covered with stratified squamous cells and is everywhere intact. Beneath the epithelium and extending up into the papillae is a cellular infiltration of lymphocytes and large mononuclear cells. These cells present a normal appearance. No cells are seen in mitotic division. It is impossible to state that this merely represents a cellular infiltration of chronic inflammation or whether these cells are an infiltration of a monocytic leukemia. From the appearance of these cells which are well preserved such a diagnosis cannot be made. Diagnosis: Fragment of skin showing chronic inflammatory reaction."

In March 1940 the patient was again seen, after a two year lapse, complaining primarily of skin symptoms accompanied by a 14 pound weight loss and insomnia. The physical examination was essentially changed in only one respect, i.e. the lymph nodes in the cervical, axillary, and inguinal regions were enlarged to the size of a robin's egg, and the spleen was barely palpable. The red blood cell count was 5.0 millions, hemoglobin 82 per cent, but the white blood cell count was found to be 47,000 with polymorphonuclears 16 per cent, lymphocytes 72 per cent, and eosinophiles 2 per cent. Of the lymphocytic series, 50 per cent were adult lymphocytes and 22 per cent lymphoblasts. At this time the microscopic slides of the skin lesions and the blood

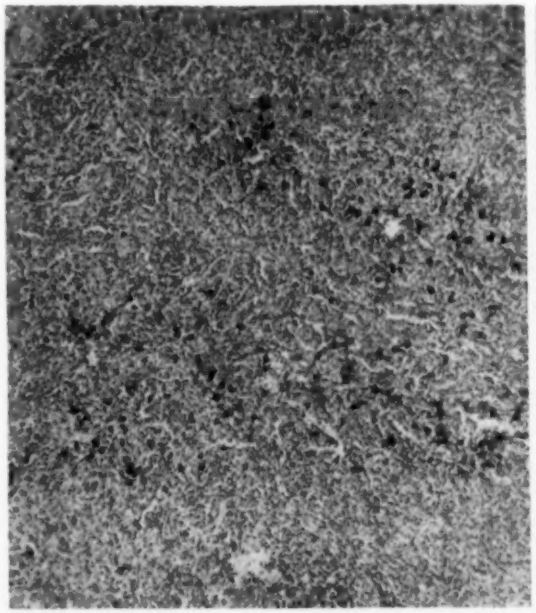

FIG. 1. Spleen: Many dark staining lymphocytes are seen in the spleen. This picture is consistent with lymphocytic leukemia.

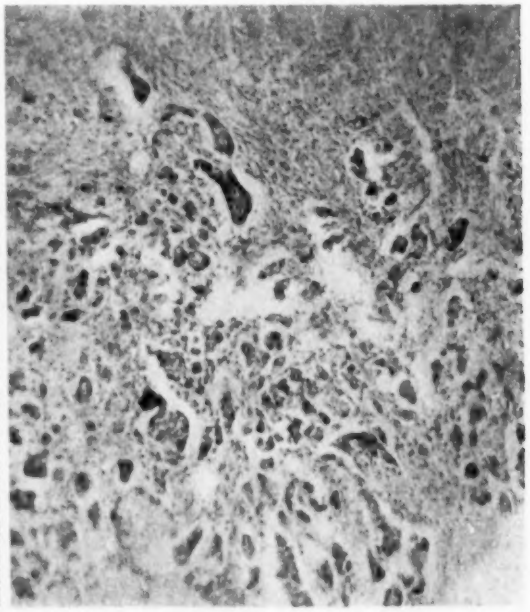

FIG. 2. Lung: This section shows the tumor cells which have invaded the lung tissue and are arranged in groups suggesting small acini. These are polyhedral endothelial cells and in many areas under high power show mitotic figures.

smears were sent to Dr. Bruce K. Wiseman of Columbus, Ohio, who felt that the peripheral blood smears showed a definite leukemia and that the skin lesion was consistent with chronic lymphatic leukemia.

In April 1940 the patient was seen at the New Haven Hospital Radiology Department where physical examination revealed a bright-red scaling dermatitis which involved the entire body including the soles, palms, and scalp. The cervical, axillary, and inguinal lymph nodes were enlarged and the tip of the spleen was felt five fingers'-breadth below the left costal margin. The legs were swollen from the knees down and showed 2-plus pitting edema. No leukemic infiltrations were noted in the fundi. A blood count showed a red blood cell count of 3.9 millions, hemoglobin of 78 per cent, and a white blood cell count of 47,000 with predominance of lymphocytes. From April 1, 1940 to May 6, 1940 she was given generalized body irradiation in nine treatments, at the conclusion of which she felt better, her white blood cell count had dropped to 18,000, but her skin condition was unimproved. In November 1940 she was again seen at that Radiology Department for the same skin condition, at which time the white blood cells numbered 47,000, so that between November 27, 1940 and December 25, 1940 she received 10 roentgen-ray treatments again with no effect on the skin condition and with a drop in the white blood cell count to 33,000. In July 1941 she returned again for a course of therapy with the skin condition at that time much worse and the white blood cells totaling 48,000. A series of eight roentgen-ray treatments was given from July 10, 1941 to July 28, 1941 which did not improve the patient's skin condition nor her general well-being, and the total white blood cell count at conclusion of therapy was 25,000.

In the fall of 1941, Dr. Charles Doan, of Columbus, Ohio, examined the patient and confirmed the diagnosis both in regard to the skin condition and the underlying leukemia. Her skin condition continued to be her chief source of discomfort, she saw several physicians and was also seen at Memorial Hospital, New York City, and all consultants stated that she had "chronic leukemia" and nothing further in therapy could be offered.

During the years 1942 and 1943 the patient received no treatment whatsoever and was not seen by any physician. However, during this period her skin condition improved greatly, and she had gained both in weight and strength. After this short period of relative well-being, she again began to get worse. For a few months before entry to the hospital she experienced frequent episodes of profound asthenia. About three days before admission, progressive exertional dyspnea and orthopnea appeared, accompanied by cough and right-sided chest pain so that medical aid was sought when respiratory distress was very marked. The past history and systemic review were non-contributory, but the family history revealed that her father died of lung cancer.

Physical examination on admission revealed a very pale dyspneic and orthopneic white female, sitting upright in bed, gasping for breath, and apparently in extremis. The pupils were equal in size and reacted well to light. No leukemic infiltrations were found in the fundi. The nasal septum was intact and no obstruction was noted. The ears, lips, mouth, and pharynx were not remarkable aside from complete edentia. A few shotty cervical lymph nodes were felt, but no other lymphadenopathy was noted. The trachea was deviated to the left. The chest showed no respiratory motion on the right side where from apex to base there was flatness to percussion, absent tactile and vocal fremitus, and absent breath sounds. The left chest was resonant to percussion and clear to auscultation with exaggerated breath sounds. Blood pressure was 140 mm. Hg systolic and 90 mm. diastolic. Heart examination revealed apex beat at left anterior axillary line, regular rhythm with tachycardia, and tones of good quality with no murmurs. The abdomen was markedly distended and tense so that nothing was felt at this time. No masses were found in the breasts. There was 2-plus edema of the lower limbs, and the reflexes were sluggish. The skin was dry and scaly, and had a brawny feel over the neck, back, abdomen, and lower extremities.

An immediate right thoracentesis was performed and 3250 c.c. of blood-tinged fluid were released, examination of which revealed small groups of peculiar polyhedral cells, suggesting tumor cells, but no mitoses were found. Similar cells were found in fluid removed on the tenth and eighteenth hospital days. The initial blood count showed a red blood cell count of 3.9 millions, hemoglobin 83 per cent, and a white blood cell count of 6,500 with polymorphonuclears 72 per cent, lymphocytes 24 per cent, eosinophiles 3 per cent, and basophiles 1 per cent. Subsequent white blood cell counts revealed similar findings, and study of the sternal marrow showed it to be active in both the granulocytic and erythropoietic series, with many more monocytes present than normal. Platelets totaled 105,000 per cu. mm. The non-protein nitrogen was 25 mg. per cent, blood sugar 95 mg. per cent, uric acid 2.6 mg. per cent, and serum proteins 5.31 gm. per cent. The Wassermann and heterophile antibody reactions were negative. The sedimentation rate was rapid. The admission urine showed specific gravity 1.025, 4-plus albumin, 4-plus acetone, and numerous white blood cells and red blood cells. A chest roentgenogram taken on the day after admission revealed a well-defined right hydropneumothorax with approximately 80 per cent collapse of the right lung, which appeared to be atelectatic; displacement of the heart and mediastinum to the left, and mottling in the left lower and midlung fields. The bony thorax was normal, and a metastatic series revealed no abnormalities. A flat film of the abdomen revealed marked enlargement of the liver with the inferior margin about 3½ cm. below the crest of the ileum, and a large spleen measuring 15 cm. by 3½ cm.

Following the thoracentesis, the respiratory distress was relieved, the patient was comfortable and the abdominal distention decreased, so that the spleen and liver were palpable. A gynecological consultant found no pelvic abnormalities. She was allowed out of bed and discharged home on February 2, 1944.

Following discharge the patient felt well for five days and then had a recurrence of rapidly progressive dyspnea and orthopnea, accompanied by profound anorexia, nausea, vomiting, asthenia, and insomnia, so that hospitalization was again ordered.

The patient was readmitted to Grace Hospital on February 9, 1944. Physical examination again revealed her to be in acute respiratory distress. The right breast was larger than the left due to dependent edema. The heart was unchanged. Over the left lower lobe there was flatness to percussion with decreased tactile and vocal fremitus, and absent breath sounds at the base, while over the right lung fields the signs of a hydropneumothorax persisted. The liver extended down to the iliac crest, and the spleen was four fingers below the left costal margin. Pitting ankle edema was present. Lichenification and scaling of the skin were noted in addition to the presence of numerous red macular lesions. A left thoracentesis was done with release of 900 c.c. of serosanguinous fluid, the examination of which showed cells similar to those seen in the fluid from the right chest on the first admission, but in addition there were mitotic figures. The blood count revealed no anemia and a normal total white count of 5,800 with 17 per cent eosinophiles and 53 per cent polymorphonuclears. The eosinophilia was present in several subsequent blood counts, but was not as marked. The urine showed 1-plus albumin and scattered red blood cells and white blood cells. A repeat chest film was taken and again revealed the right hydropneumothorax with collapsed right lung, while in the left mid-lung area small mottled opacities were noted with a small left pleural effusion. Despite all supportive measures and repeated thoracenteses, the patient rapidly grew worse and died on March 1, 1944.

Autopsy Findings. The body was that of a fairly well-developed, undernourished, pale white female, measuring 63 inches in length. Rigor mortis was absent, but postmortem lividity was present.

On opening the abdominal cavity a somewhat larger amount than normal of peritoneal fluid was present which was clear and straw-colored. The liver was found to extend nine fingers'-breadth below the right costal margin. The dome of the dia-

phragm on the right side was at the level of the sixth rib, while on the left side it was at the level of the seventh rib. The spleen extended three fingers'-breadth below the left costal margin.

On opening the thoracic cavity the mediastinum was found to be shifted somewhat to the left, away from the midline, and fixed in this position by abnormally thick fibrous adhesions. The right pleural cavity was completely filled with bloody fluid. The left pleural cavity contained a smaller amount of bloody fluid and the pleura here was somewhat thickened. In place of the right lung was an elongated structure about 17 cm. in length which extended down to the diaphragm with which it became incorporated. At the lower part just above the diaphragm this measured about 4 cm. transversely and higher up about 7 cm. It was about 4 cm. thick. It consisted of firm white tissue apparently representing the tremendously thickened pleura, and in the center of this mass was the remains of the compressed right lung. The peribronchial lymph nodes were somewhat enlarged and quite hard. On section of this compressed lung, no tumor growth was found in the lung tissue except small lymph nodes which appeared to be involved. The left lung showed collapse of the lower half of the lower lobe, and there were some grayish nodules attached to the pleura here. The upper lobe was fairly well-expanded.

The diaphragm was very much thickened, most markedly on the right side, where it measured as much as 12 mm. in thickness. A thin muscle layer could be recognized in the center of this, but on both surfaces there was compact grayish tissue. This was particularly hard on the undersurface of the diaphragm.

The heart weighed 265 grams. The pericardial fluid was somewhat increased in amount and was blood-tinged. The superficial vessels were somewhat tortuous, showing that the heart had been larger. The orifices were of normal size. One cusp of the mitral valve showed some grayish thickening. The myocardium showed nothing of particular note. The coronary arteries were smooth.

The spleen weighed 315 grams. It was smooth on the surface, and the capsule was not thickened. On section it was moderately firm and showed considerably enlarged malpighian bodies, a picture which would be consistent with lymphatic leukemia.

Gastrointestinal tract. Near the cecum there was a mass of firm adhesions binding the intestines together, and there was here a very firm area attached to the retroperitoneal tissue. The stomach showed nothing of particular note. Along the course of the small intestine there were minute hard nodules at the mesenteric attachment. The appendix was present. Very near the attached end of the appendix was the firm tissue described above, which on section suggested the possibility of a small tumor. This did not involve the mucous membrane in the gross. No tumors of the mucous membrane were found.

The pancreas appeared normal.

The liver weighed 1,570 grams. It was smooth on the surface with some thickening of its capsule on its anterior surface. On section the liver showed no definite abnormality. No tumor nodules were found in it. No calculi were present in the gallbladder.

The adrenal glands showed nothing of particular note.

Kidneys: Combined weight 240 grams. Capsules stripped a little less readily than normal, but left a smooth surface. The cortex was rather pale and somewhat thinner than normal. The pelvis of the right kidney was a little dilated.

A few somewhat enlarged lymph nodes were found in the abdomen.

The abdominal aorta and its main branches showed no arteriosclerosis.

The uterus was small and showed nothing of note. The ovaries had some small cysts and one of them had a small solid grayish nodule suggesting tumor growth. The bladder was apparently normal.

Anatomical Diagnosis. Marked chronic thickening of pleura with encasing of right lung. Bilateral hemothorax. Partial atelectasis of left lower lobe. Chronic thickening of diaphragm. Old peritoneal adhesions with questionable tumor. Numerous small retroperitoneal nodules attached to the intestine. Moderate enlargement of the spleen with hypertrophy of the malpighian bodies. A few enlarged lymph nodes.

From the gross findings the one thing which suggested lymphatic leukemia was the appearance of the spleen. The condition in the chest and the diaphragm, and the firm peritoneal adhesions were difficult to explain on this basis as their etiology was not evident from these gross findings.

Microscopic Examination. A malignant tumor growth was found in the thickened pleura of the right lung, in the small nodules in the pleura of the collapsed lower lobe of the left lung, peribronchial lymph nodes, the diaphragm, the adhesion of the cecum near the appendix, the minute nodules in the mesentery of the small intestine, the retroperitoneal lymph nodes, and the ovary. The type of tumor was apparently the same in all these locations. As seen in the thickened pleura of the right side, the tumor growth showed spaces lined with cells with much compact fibrous tissue between these spaces. The cells lining these spaces varied in shape, some being quite flat, but others were cuboidal and approaching the columnar type. To this extent they resembled a glandular growth. Where the cells of the tumor were more numerous, as in the lymph nodes, there was no definite arrangement. From the appearance of the cells of the tumors, the classification is difficult. The possibility of a malignant carcinoid was considered and a section was stained by the argentaffin method with negative results. From the distribution of this tumor growth, involving as it evidently had for a long time the right pleura and diaphragm, it seems most probable that this was primary in the right pleura, and is an endothelioma. It was evidently slow growing as shown by the large amount of compact fibrous tissue in the right pleura and diaphragm. In sections of the right lung, minute areas of tumor were found in the lung tissue, but these in all probability were metastatic and the growth was not primary here. In sections of the proximal end of the appendix and adjacent tissue, the tumor growth was found extending up to the outer part of the mucous membrane. Although it is a most unusual picture, in my opinion, as given above, it is an endothelioma.

The heart showed no definite abnormality.

Lungs: In addition to the tumor growth, the right lung was much collapsed as was also the lower lobe of the left lung. Sections of the left upper lobe showed air spaces better expanded, but with numerous pigment-containing cells resembling heart-failure cells.

The spleen showed large malpighian bodies with a considerable number of small round cells in the stroma between these.

The pancreas showed no definite abnormality.

Liver: Nothing suggesting tumor growth was seen, and there was no collection of lymphocytes between the columns of liver cells.

Kidneys: In some fields there were numerous small cells, but these had the appearance of developing connective tissue cells and not lymphocytes. In most areas these cells were lacking.

Skin: Sections showed some small groups of round cells under the epithelium, indicating a chronic inflammatory process here.

Bone Marrow: Sections of a rib showed normally active marrow.

Regarding the presence of any lesions indicating lymphatic leukemia, the appearance of the spleen would be consistent with, but not diagnostic of this condition. The other organs, particularly the liver and kidney, did not show the lymphocytes one expects to find in that disease.—Dr. Charles J. Bartlett, Pathologist, Grace Hospital, New Haven, Connecticut.

Discussion

The case recorded above is by all available criteria typical of a pleural endothelioma from both the clinical and pathological standpoints. The symptomatology and physical findings were classical for a fully-developed case. The initial thoracentesis gave transient relief of the dyspnea and orthopnea, but rapid reaccumulation of the fluid took place and subsequent chest taps provided little or no palliation. The fluid was always hemorrhagic and on several occasions mitotic figures were present on microscopic examination of the sediment, suggesting tumor cells. Thoracentesis was difficult owing to marked pleural thickening. Roentgenographic examination of the chest following the creation of an artificial pneumothorax revealed no evidence of pleural tumor nodules, but did show the atelectasis of the right lung and the shifted mediastinum.

In the contralateral lung several areas of mottling were found on roentgenogram which at autopsy proved to be tumor nodules in the lung septa. Careful examination of the lungs and bronchi failed to reveal evidence of bronchogenic carcinoma. The terminal picture is primarily due to the pleural endothelioma with widespread metastases rather than to the underlying leukemic condition, as the only evidence remaining at autopsy of her previous leukemia was the presence of enlarged malpighian corpuscles in the spleen.

The original complaint for which the patient consulted her physician was a chronic exfoliative dermatitis which some time after its onset was accompanied by a marked leukocytosis, the differential count showing a marked predominance of lymphocytes and lymphoblasts. At first it might appear that the patient had a primary skin disease with an associated leukemoid reaction. However, the clinical course during the next few years with marked generalized adenopathy, splenomegaly, and persistently elevated white blood cell counts with predominance of lymphocytes and lymphoblasts rules against such a supposition. Furthermore, the diagnosis of leukemia was confirmed by Drs. Charles Doan and Bruce Wiseman of Columbus, Ohio, by Dr. C. P. Rhoads of Memorial Hospital, New York City, and at the New Haven Hospital Out-Patient Department. A leukemoid reaction in association with neoplasm has been reported by several authors [20, 21, 22, 23, 24, 25]; however, this condition occurs when metastases are present in the bone marrow and spleen and is usually a terminal event.

Because of the duration of this patient's illness following the onset of her elevated white blood count it is inconceivable that this represents a leukemoid reaction to a neoplasm since statistics show that life expectancy in patients with pleural endothelioma is two years or less on the average. Furthermore, the presence of a normal sternal marrow and peripheral blood smears at her last admission rules against metastatic bone marrow involvement. At autopsy the spleen did not show metastatic involvement, but rather findings consistent with lymphatic leukemia.

The most intriguing point in this case aside from the association of a rare neoplasm with leukemia is the paucity of evidence of chronic lymphatic leukemia at autopsy. Forkner [1] has stated that in a small proportion of patients with chronic leukemia temporary improvement may occur for weeks or months, whereby the leukocyte count may be reduced and organs decrease in size, these changes being independent of any particular form of treatment. Such reactions would appear to represent possible spontaneous remissions. Furthermore, in

some cases following roentgen-ray therapy a definite decrease in the white blood count and in liver, spleen, and lymph node enlargement does occur. A few authors [26, 27, 28, 29] have observed spontaneous remissions in untreated cases, but no examples of anything approaching complete spontaneous remission of chronic leukemia has been recorded, although Doan and Wiseman [30] and others have reported that patients with chronic lymphatic leukemia may live many years and die of totally unrelated causes. Numerous authors, Minot and Isaacs,[31] Arendt and Gloor,[32] and others have reported improvement and even moderate remissions in patients treated with roentgenogram. It would appear, however, in our case either that roentgen-ray therapy produced an unusually long remission with disappearance of the characteristic clinical-pathological findings, or else a true prolonged spontaneous remission occurred, either of which is indeed extremely unusual.

If one subscribes to the point of view that leukemias are neoplastic in origin and that occurrence of a second neoplasm, not metastatic, frequently inhibits the growth of the first one, then it is also not inconceivable that the leukemic remission in this case was caused by such a mechanism.

Summary

A case of primary endothelioma of the pleura with widespread metastases in a patient with chronic lymphatic leukemia is reported.

The pathology, clinical course, and roentgenographic findings of pleural endothelioma are reviewed.

The leukemic picture in our patient antedated the malignant process in the pleura and apparently played no part in the terminal picture, as is evidenced by the paucity of lesions of lymphatic leukemia at autopsy.

The possibility that irradiation therapy had produced a prolonged remission in the leukemic state is discussed.

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FRIEDLÄNDER'S BACILLUS MENINGITIS WITH REPORT OF CASE TREATED UNSUCCESSFULLY WITH SULFADIAZINE *

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Meningitis due to Friedländer's bacillus, a rare medical entity, was first described with a reported case by Weichselbaum [1] in 1888, six years after Friedländer's original description of the organism. In 1931, Rothschild [2] found in the American literature only a single case of Friedländer's meningitis and this one ended fatally.[3] Rothschild's case, the second American case reported, according

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to Ransmeier and Major [4] is the only incontestable non-fatal case, prior to sulfonamide therapy, of purulent meningitis in which Friedländer's bacillus was recovered from the spinal fluid and adequate details of its bacteriologic identification given. Recovery in this case followed adequate surgical drainage of a subdural abscess secondary to bilateral otitis media and mastoiditis. Commenting on Carcelli's [5] review of 12 cases in the literature with three reported recoveries, Rothschild [2] found that in the recovered cases the bacteriologic diagnosis was not satisfactorily confirmed.

MacKay,[6] quoting Neal's [7] statistics, found six cases of meningitis due to Friedländer's bacillus in 3599 cases of meningitis in the New York area. Finland and Dingle,[8] writing in the Medical Progress series on treatment of meningitis, list one reference [15] of Friedländer's bacillus meningitis, a case which recovered with sulfapyridine. Yaskin [9] studied meningitis as a complication of nasal or aural disease and found that 58 of 123 cases of meningitis in general hospital practice originated as a complication to nasal or aural disease. Staphylococcus, pneumococcus and streptococcus predominated and the one case of Friedländer's bacillus meningitis listed was of systemic rather than of nasal or aural origin.

MacKay and Morris,[10] reported a case of bacillus Friedländer meningitis secondary to prostatic suppuration. Localization of Friedländer's bacillus infection in 198 cases as studied by Baehr, Schwartzman and Greenspan [11] is disclosed in the following table.

Gastrointestinal tract	30%
Genitourinary tract	25%
Biliary	23%
Lungs and upper respiratory tract	12%
Muscle, skin and meninges	5%
Vagina, uterus	3%

In 1942 Ransmeier and Major,[4] in reporting their case and reviewing the available literature, were able to collect data on but 30 cases of meningitis caused by encapsulated bacilli of the Friedländer group. Four of these reports are from the United States,[2, 12, 13, 14] one from Canada,[15] and one from Cuba,[16] and the rest from European journals (see 4 for references). Their summary well characterizes the Friedländer bacillus meningitis. The disease occurs chiefly in infants and in adults, often after the fourth decade. A primary focus, as determined by the recovery of the Friedländer bacillus there simultaneously with its recovery from the spinal fluid, was present in the middle ear, mastoid and sinuses in over half the adults while in the majority under three years a primary focus was undetermined. Pneumonia was a precursor in five cases. Cholecystitis, arthritis, uterine infection and pharyngitis are mentioned. Elsewhere prostatic suppuration is mentioned.[10] Six of the adults had diabetes, one cirrhosis of liver, others were alcoholics, two infants had congenital syphilis and two had intracranial hemorrhage—all of which suggested that debilitating conditions may predispose to the development of Friedländer's bacillus meningitis. The diagnosis is dependent upon finding in the smear and in the cultures of the spinal fluid the organisms fitting the description of Friedländer's bacillus. Friedländer's bacillus meningitis simulates that due to the meningococcus in its tendency to the development of petechiae and the likely absence of organisms on direct smear of the spinal fluid. Five of 19 cases had negative direct smears. Culture of the

first spinal fluid was positive in 15 of 17 cases. The fluid has the characteristics of a purulent meningitis with many polymorphonuclear leukocytes present, increased protein and low sugar. Of 10 cases having blood cultures, five were positive and all died. Of five with negative blood cultures two survived.[15, 2] Prior to the advent of the sulfonamides, meningitis due to the Friedländer bacillus (with one exception [2]) was invariably fatal; since then four cases are reported as cured, two with sulfapyridine [15, 16] and two with sulfadiazine.[17, 18] Sulfapyridine is, therefore, somewhat effective but sulfadiazine is the drug of choice in the treatment of Friedländer bacillus meningitis.[19, 20, 13]

Principally because of the rarity of the above described medical entity—formerly considered invariably fatal but now with some hope of cure with sulfonamide therapy—I present the clinical and pathological details of the following case which failed to recover with sulfadiazine therapy, and in which the precise bacteriological diagnosis was made post mortem.

Case Report

This six month old white infant was first brought to my office August 14, 1944 because of an illness of several days characterized primarily by diarrhea but also by vomiting, cough, fever and irritability. Two days earlier a physician elsewhere had given the baby medication for the diarrhea but without improvement. History disclosed that the patient, although somewhat pale from birth, had never been significantly ill. He had developed and grown normally from all appearances. He had been delivered elsewhere at term by an elective Caesarean section, seven days after which the mother died, apparently of intestinal obstruction. This baby was from the sixth pregnancy. Offspring one, two and four were living and well whereas number three died shortly after birth from spina bifida and number five died at three months of pertussis. Physical examination disclosed an acutely ill, lethargic, pale infant with rapid pulse, respirations of 50 to 60, and a rectal temperature of 104° F. There was moderate mucopurulent nasal discharge, negative ear drums, moderately infected throat with slightly dry mucous membranes. There were scattered râles in the lungs, especially in the lower right lung. The abdomen was neither distended nor tender. The neck was not stiff, and there was no Kernig reaction. A diagnosis of a respiratory infection, probably pneumonia, was made, and the gastrointestinal picture was considered as a secondary manifestation.

Inasmuch as the infant had not vomited for over 24 hours, it seemed that oral fluids and medication would be satisfactorily tolerated. The following orders were given: 1. Diet as tolerated of equal parts of boiled milk and water. 2. Sulfadiazine, 0.5 gram at once, 0.25 gram in one hour and thereafter 0.25 gram every four hours, crushed and mixed with teaspoonful of Karo syrup. 3. A tablet consisting of 0.015 gram of phenacetin and 0.060 gram of acetylsalicylic acid was to be given every three to five hours as needed for restlessness. Twenty-four hours later it was found that the above orders were carried out uneventfully but without improvement, especially of the diarrhea, which seemed of greatest concern to the attendants. Temperature was 103° F. rectally. Sulfadiazine was increased to 0.5 gram every four hours. After another 24 hours, now 48 in all with adequate sulfadiazine clinically, there was still no apparent improvement. (There was no practical method available in this rural situation to determine whether the blood level of sulfadiazine was adequate, but the above doses, checked by counting tablets, were given and the baby, by report, had not vomited during this time.) The baby, now for the first time, refused oral medication and nourishment. He seemed more lethargic, with suggestive stiffness of the neck and with depressed fontanelles, all of which were considered mani-

festations of further dehydration and he was hospitalized forthwith, primarily to restore the fluid balance and for whatever other treatment seemed indicated.

The infant promptly went into coma with temperature 102.6° rectally, pulse 160, and respirations 60. The left side of the body seemed more rigid than the right. The neck was moderately stiff. The signs in the lungs were unchanged. Respiratory distress, including cyanosis, was not as significant as the gravity of the general picture presumably from a complicating meningitis.

Laboratory examination showed the urine to be acid, straw colored, with cloudy test for albumin, negative test for sugar and urates and epithelial cells in the sediment. There was a trace of acetone. Red cell count was 4,180,000 with 52 per cent hemoglobin. White cell count was 53,600 with 64 per cent polymorphonuclear leukocytes, 6 per cent myelocytes, 20 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophiles. By spinal puncture, only about 2 c.c. of blood were obtained. (It is unlikely that the spinal canal was penetrated.)

Following the administration of 1,000 c.c. of normal saline solution by hypodermoclysis in two 500 c.c. doses over a period of 36 hours, the infant developed generalized edema, particularly evident in the facies and in the scrotum. Twelve hours before death, a Levene stomach tube was passed. The fasting contents of the stomach had a sticky grayish green appearance but they were not studied microscopically. Along with three ounces of boiled water 1.0 gram of sulfadiazine in a single dose was administered. Also, the formula, in two ounce quantities, was given twice before a recurrence of vomiting occurred. The patient's temperature was between 98° and 99° F. during the last 36 hours, but there was very little change in pulse and respirations. Oxygen was not given, inasmuch as the small degree of cyanosis as well as the but slight to moderate respiratory difficulty seemed less significant than the dehydration and infection. There was no diarrhea throughout the hospital stay of three and one-half days. Six days after I first saw the infant and after at least 10 days of illness treated as outlined, the patient died. Clinical diagnosis was pneumonia complicated by meningitis with the causative organism undetermined before death.

Autopsy Findings. The autopsy findings of importance were bilateral bronchopneumonia, catarrhal ileocolitis with gaseous distention of the entire gastrointestinal tract, lymphoid hyperplasia of the spleen, cloudy swelling of the liver and kidneys, and diffuse lepto-meningitis. Cultures taken from the subarachnoid fluid, the heart's blood and the contents of the ileum showed a gram negative bacillus having the cultural characteristics of Friedländer's bacillus.

The pathologist * wrote: "In reviewing the history, it is my opinion that the enteritis previous to the present illness probably was the predisposing factor in the onset of the terminal disease. Although Friedländer's bacillus is occasionally found in the intestinal tract as a pathogen, it is more commonly found in the respiratory tract and, in view of the fact that a well established bronchopneumonia was found in both lungs, I believe that the pneumonia, the bacteremia and the lepto-meningitis were the result of a complicating secondary infection terminating fatally. It would be fair to assume that the primary infection with the Friedländer organism probably occurred in the lungs. The changes in the heart, liver, spleen and kidneys are secondary to the toxemia of infection."

Bacteriological Findings. Cultures taken from the small bowel, heart's blood and subarachnoid fluid revealed a gram negative bacillus having the cultural and morphological characteristics of Friedländer's bacillus, as verified by the State Department of Health laboratories.†

The bacteriological findings were gram negative, encapsulated diplo-bacilli which grew at room temperature, at 37° C., aerobically and under slightly decreased oxygen

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tension on a variety of media including Loeffler's blood serum, blood agar, dextrose agar and in broth. On solid media the colonies were moist, confluent and blue gray. The organism fermented dextrose, sucrose and lactose. Although it is not of differential diagnostic importance the organism also fermented maltose and mannitol. A guinea pig injected intraperitoneally, with a 24 hour culture, died within 18 hours. The peritoneal exudate was stringy and the organism recovered morphologically resembled the one introduced into the peritoneum.

Summary

Friedländer's bacillus meningitis as reported, particularly in the American literature, is exceedingly rare. It has a predilection to occur in infants and in adults past middle age. Although formerly considered invariably fatal, meningitis due to Friedländer's bacillus in recent years has occasionally been cured with sulfapyridine or sulfadiazine, the latter being the more effective. The case report of this paper is of an infant treated adequately clinically with sulfadiazine but without success. Autopsy studies confirmed the diagnoses of bronchopneumonia, ileocolitis and meningitis with the causative organism proved to be the Friedländer bacillus.

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APLASTIC ANEMIA FOLLOWING EXPOSURE TO PRODUCTS OF THE SULFITE PULP INDUSTRY: A REPORT OF ONE CASE*

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This case presents many features of interest. The disease is uncommon and rarely seen by the general practitioner. No report in the literature has been found in which a case of aplastic anemia may have been caused by exposure to products of the sulfite pulp industry. The history revealed that symptoms of intoxication were present for some 17 months prior to seeking medical aid.

The patient for some 20 years was manager of a pulp and paper company which makes paper pulp by the Mitscherlich or sulfite process, in which wood chips and calcium bisulfite enter large digesters or autoclaves and emerge finally as sulfite pulp. He was almost daily exposed to fumes at times of high concentration in closed areas and was constantly handling and frequently seen chewing pieces of sulfite pulp.

Many industrial studies have been made of the toxicological effects of the more commonly used chemicals. Such studies will not of necessity apply directly to the paper industry in which the contaminating chemical substances are not clearly identified and the actual amounts of toxic constituents may be so small as to be estimated with difficulty.

Among the possible toxic materials in a sulfite pulp mill are the relief gases from the digester. Investigations of the oil soluble constituents of relief liquor from the pulp mill have revealed some interesting findings. The oil-soluble fraction in relief liquor represents about 4.5 parts in 12,000, of which about 90 per cent is para cymene. Cymene is a substituted benzene and as such is an irritant. According to Woronow (1929),[1] cymene closely resembles pseudo cumene in its effects, and it does not exhibit the tendency, shown by benzene to cause anemia and leukopenia; similar results were reported by Miyamoto (1937).[2] Cymene (cymol), methyl isopropyl benzene, can exist in the form of three isomers, of which only the para compound has been studied toxicologically. Other constituents of relief liquor are: sulfur dioxide gas, acetaldehyde, acetone,

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methyl alcohol, acetic acid, formic acid and terpenes. Of these constituents, aside from benzene, acetone has been found after continued inhalation to cause a destruction of the red cells and hemoglobin, and may produce chronic tissue damage in high concentrations. These irritants either singly or in combination were probably important etiological factors in this case. The effect of cymene and the other related terpene derivatives in the exhaust gases from the sulfite industry has not been demonstrated.

The effects of benzene poisoning have been extensively studied. The following recent articles contain points of special interest.

Hunter [3] reported a study of 89 individuals exposed to benzene fumes and said that marked variations in individual susceptibility exist and suffice to explain why in the same concentration of fumes one individual is poisoned and another is not. According to his observations the first clinical symptoms and signs of chronic poisoning may appear long after exposure has ceased. Selling and Osgood [4] collected from the literature 54 cases of aplastic anemia in whom symptoms developed from two weeks to 35 years after exposure. The average was one year or less. Hunter [3] observed that benzene may bring about: polycythemia or anemia; leukocytosis or leukopenia; leukemia or leukemoid blood pictures (either lymphatic or myeloid); eosinophilia; megalocytosis or microcytosis; the presence of immature marrow elements in an otherwise normal blood. This author questions whether any concentration of benzene greater than zero is safe over a long period of time.

Greenburg et al.[5] report that the symptoms of early benzene poisoning, such as weakness, fatigue, epistaxis, dryness of the throat, loss of appetite, nausea, dizziness, insomnia, lethargy and dermatitis, may or may not be present in persons with serious blood changes, characteristic of benzene intoxication.

It seems probable that many cases of intoxication occur in the paper industry but are not recognized.

Case Report

History. C. K. B., a white male aged 56 years entered St. Elizabeth Hospital, Appleton, Wisconsin, on December 5, 1942. He had been in good health until July 1941 when he began complaining of progressive weakness and lassitude. He noticed a palpitation of his heart and dyspnea upon any exertion. He especially noticed that any bump would produce bluish areas on his skin. At intervals a slight epistaxis was present coming from the left nostril. There was no history of any acute infection or sore mouth, no intake of drugs and no dietary deficiency.

The past history was negative for any hemorrhagic phenomena except the areas of ecchymosis when he bumped himself. There was no family history of blood dyscrasia, and the history was otherwise negative.

Physical examination upon admission revealed a well developed and well nourished middle aged male who did not appear acutely ill. There was a marked pallor of the skin. The temperature was 99.2° F., pulse 72, respirations 20, and the blood pressure 140 mm. Hg systolic and 90 mm. diastolic. There was present a soft diastolic murmur in the auscultation area of the aortic valve which was presumably a result of the severe anemia. Worthy of note was the absence of splenomegaly, lymphadenopathy, and absence of any internal bleeding. The examination of the prostate was negative and the roentgenogram of the pelvic bones showed no malignancy. Scattered over the palate and lower extremities were numerous petechiae of varying sizes. Areas of ecchymosis were present over the left arm and right upper eyelid, the latter

coming from rubbing his eye. No evidence of stomatitis or hemorrhages under the finger nails was present.

Laboratory Findings. The urine was negative except for an occasional erythrocyte and leukocyte. The stool examination was negative for macroscopic or microscopic blood.

The non-protein nitrogen was 31.6 mg. per cent, blood sugar 100 mg. per cent. The Kahn reaction was negative. Roentgenograms of the chest and the gastrointestinal series were negative. The result of the fractional test meal was as follows: The first 15 minutes, free HCl 0°. In 30 minutes free HCl 0°. Histamine 1 c.c. was

TABLE I

Transfusions and Results of Blood Examinations

Illness Day	Amt. of transfusion c.c.	R.B.C.	Hgb. % grams	W.B.C. Total	Reticulocytes	Polys %	Lymphocytes %	Platelets	Hemorrhage	Bleeding Time Min.	Clotting Time Min.	Comment
1	500	1.6	4.5	1,450	0.5	34	81	638	+			
2												
3		1.9	7.1	2,200		41	58		+			
4												
5	500											
6												
7										0	6	
8		2.6	7.3	2,500		24	76		+			
9												
10												
11		2.1	6.9	1,800		23	75		+			
12	500											
13												
14												
15												
16												
17		2.9	10	2,000		12	84		++			
18	500											
19		3.7	10	1,700		16	84		++			
20+												
34 −		2.4	7.6	1,100		24	76		++			
35	500	3.2	8.4	2,200	0.7	20	79	1,700	++			
36												
37		3.2	9.4	1,800		12	86		++			
38												
39												
40												
41	500	3.0	8.4	1,100		22	78		+			
42												
43												
44		2.6	8.0	1,500		9	91		+			
45												
46												
47	500								++			
48												
49++												
50		2.08	9.6	1,600	0.6	16	76	0		0 − ½ hr.		
51												
52												
53					0.2							
54					0.2							
55		3.45	10.6	1,000	0.5			70,000				
56												
57												
58		3.04	10.2	2,400	0.2			289,000				
59					0.2			153,000			5	No clot retraction
60		3.18						25,000				in 24 hrs.
61												
62		3.00		1,000				11,000				
63												
64												
65		2.56		900				12,000				
66												
67		3.37		1,200								Eight transfusions
68												of 500 c.c. given 49th to 67th day.

\+ Day of discharge from hospital.
− Returned to hospital.
++ To Mayo Clinic.

given. In 45 minutes free HCl 0°. In 60 minutes 11° combined and total acid 22°.

Petechiae became evident on application of the blood pressure cuff for five minutes at 120 mm. of mercury.

Laboratory studies were important in establishing the diagnosis. The results of the examinations of the blood and bone marrow are given in table 1 and figures 1 and 2.

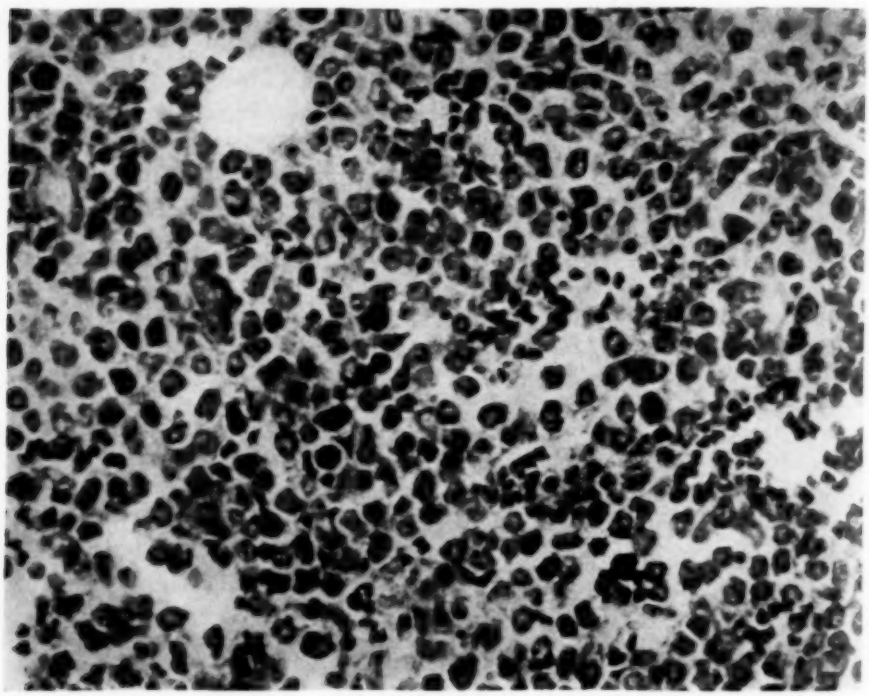

FIG. 1. Bone marrow (vertebral): The sinusoids are widely dilated and filled with normoblasts, erythroblasts, and stem cells. The marrow fat has disappeared. (500 ×.)

Clinical Course. The patient's condition varied but little. He was placed on strict bed rest and during his stay in the hospital seven blood transfusions by the citrate method were given. The medication consisted of ample doses of liver extract, ferrous sulfate and Armour's yellow bone marrow. The diet was high in protein with added vitamin C and orange juice to insure adequate vitamin intake.

The symptoms during his stay in the hospital were those principally of an active progressive anemia with a marked lowering of all the blood elements. Bruises at the site of slight bumps and spontaneous petechiae were present. Only minor areas of infection were present in the mouth. In spite of repeated transfusions the blood showed a downward trend. After his admission to the Mayo Clinic he was given eight additional blood transfusions but gradually grew weaker, hemorrhagic phenomena became more marked including bleeding from the gums and nose and from the urinary tract, and finally, necrotic ulcers appeared on the buccal mucous membranes, tongue and throat. Sulfathiazole powder failed to control the progress of the areas treated. The throat lesion gradually grew more extensive and swallowing became difficult. He died of a cerebral hemorrhage.

Necropsy. On external examination the body was extremely pale. There were many petechiae and ecchymoses measuring from pin point size to 2 cm. in diameter scattered over the body, particularly along the parasternal line and the left costal margin, the upper thighs and the antecubital spaces. There was a larger ecchymosis measuring 3 by 3 cm. over the lateral aspect of the left gluteal region. No edema, jaundice or emaciation was noted.

The peritoneal cavity contained 300 c.c. of straw colored fluid. The intestinal coils were free. The liver margin was flush with the right costal margin in the mid-

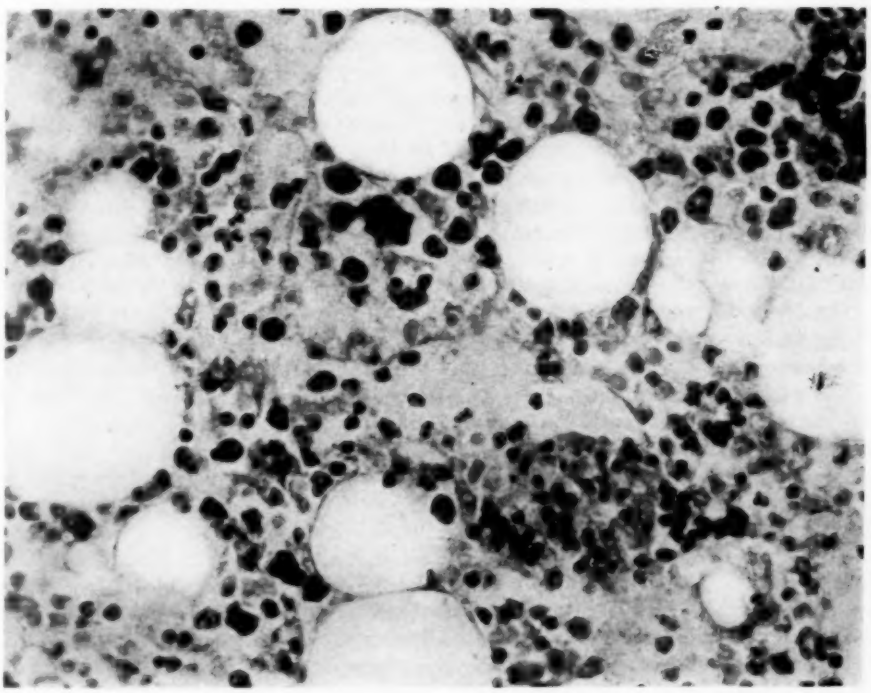

FIG. 2. Bone marrow (sternum): The fat has greatly disappeared. The marrow is scant. Numerous normoblasts and erythroblasts are present. A few maturing late normoblasts are present. (500 ×.)

clavicular line and was 2 cm. above the xiphoid in the midline. The right pleural cavity contained 100 c.c. of clear, straw colored fluid, and the left pleural cavity contained 50 c.c. of a similar fluid. There were no adhesions.

The thymus was grossly replaced by adipose connective tissue. Throughout this fat were many petechial hemorrhages.

The heart weighed 449 gm., and was pinkish brown in color with epicardial fat increased grade 1. Over the surface of the heart there were numerous petechiae from pin point to 1.5 mm. under the visceral pericardium. There was a soldier's spot measuring 2 by 0.9 cm. at the base of the right ventricle posteriorly. There was no streaking.

The appendages and valves appeared normal. There was a 2 mm. petechial hemorrhage on the ventricular aspect of the left ventricular wall which on section of the septum was also seen penetrating at least 0.6 cm. The foramen ovale was closed. Coronary sclerosis was graded 1 plus. No thrombi were present.

The cardiac measurements were: aortic valve 7.4 cm., mitral valve 10.5 cm., tricuspid valve 11.5 cm., pulmonic valve 7.2 cm., depth of left ventricle 7.8 cm., thickness of left ventricle 1.4 cm., depth of right ventricle 9 cm., and thickness of right ventricle 0.3 cm.

The upper lobe of the right lung was pink in color with anthracosis grade 1, apical scarring grade 1 and no atelectasis. Consistency, crepitation, frothing and vessels appeared normal. No edema was noted. The color of the cut surface was pink. Throughout the substance and subpleural aspect of the lung and beneath the mucosa of the bronchi were numerous pin point to 1 mm. petechiae. The right middle lobe answered essentially the same description. The right lower lobe was also similar to the right upper lobe, except that the consistency was increased grade 1 and crepitation decreased grade 1. There was a 2 cm. fresh hemorrhage in the right lower lobe on the anterior aspect near the interlobar fissure. The lobes of the left lung answered essentially the same description. There was no Ghon complex nor calcified hilar nodes present.

The spleen weighed 149 gm. and was slate gray in color with grade 1 lobulations and normal consistency. Wrinkling, trabeculae and scrapings appeared normal. There was no perisplenitis. The cut surface was red. Follicles were increased grade 2. There were two accessory spleens measuring 0.9 cm. and 0.4 cm. respectively, and situated in the tissue surrounding the tail of the pancreas.

The liver weighed 1909 gm., and was reddish brown. There were two 4 cm. diaphragmatic grooves on the upper surface of the right half of the liver. The consistency was normal. The cut surface was brown, and the markings were distinct.

The gall-bladder contained 10 c.c. of greenish bile. The wall measured 0.1 cm. in thickness, and cholesterosis grade 2 was present. There were no stones.

The bile ducts were patent and not dilated.

The esophagus appeared normal. The stomach was estimated to contain 200 c.c. of gas and blackish, bloody material. The rugae appeared normal. Throughout the mucous membrane there were diffuse, scattered, petechial hemorrhages. No ulcer was seen. The pylorus was competent. The contents of the duodenum were light yellow in color. The mucous membrane appeared normal, and no ulcer was present. The A.P. distance was 7.5 cm. Throughout the small and large bowel there were hundreds of petechiae and ecchymoses measuring up to 1 cm. in greatest diameter. There were two polyps at the splenic flexure. One of these polyps measured 0.5 cm. and had a 0.2 cm. pedicle. The other one was sessile and measured 0.5 cm. in diameter. There was melanosis of the cecum grade 2. No diverticulum was seen.

The pancreas was estimated to weigh 80 gm., and appeared normal. Both adrenal glands appeared normal.

The right kidney weighed 106 gm. The capsule stripped with ease revealing a smooth, pink surface. The consistency was normal. Lobulations were increased grade 1. Stellate veins appeared normal. There were numerous, tiny scars or pits over the surface of the right kidney. There were several 0.2 cm. retention cysts present. The cut surface was pink and the markings were distinct. The cortex measured 0.5 cm. and the medulla 1.4 cm. There was hemorrhage into the peripelvic fat. The pelvis, calices and ureter were filled with old hemorrhage, and there was grade 1 dilatation of the pelvis. The pelvis and ureter were not opened at this time.

The left kidney weighed 385 gm., and answered essentially the same description as the right kidney except that there were two 0.2 cm. scars present on the surface and three 0.2 cm. retention cysts. The cortex measured 0.7 cm. and the medulla 2 cm.

The bladder contained 300 c.c. of bloody urine. It was not dilated. The wall appeared normal. The mucous membrane showed multiple, diffuse ecchymoses present. The perivisceral tissues were also infiltrated with a diffuse hemorrhage. The trigone and ureteral orifices appeared normal.

The prostate measured 3 by 2 by 3 cm., and appeared normal. There was a 10 c.c. hydrocele on the right. Testicular stringing appeared normal.

The breasts were of the normal type.

The thyroid gland weighed 31 gm. The consistency was increased grade 2. There was a diffuse hemorrhage into the right lobe of the thyroid.

Aortic sclerosis was graded 1.

The spinal alignment was normal, and there were exostoses present grade 1.

The brain weighed 1575 gm. The external surface of the brain exhibited an occasional small subarachnoid hemorrhage, the largest being in the left temporal lobe. The sectioned surfaces of the brain revealed a hemorrhage into the substance of the pons with destruction of the major portion and also obliteration of the aqueduct of Sylvius. The hemorrhage extended into the third and fourth ventricles, with infarction of the floor of the fourth ventricle. The left internal capsule also exhibited numerous discrete and confluent small hemorrhages with marked softening of this area. The hemorrhage from the third and fourth ventricles extended into the left lateral ventricle for approximately 1 cm. These hemorrhages were composed chiefly of recently clotted blood and fluid blood. The cerebral sclerosis was estimated to be grade 1. The bony structures at the base of the skull were normal. The spinal cord appeared normal.

Bone Marrow: Ribs and sternum showed no fat and a barely evident background of thin fibrous stroma. Cellularity was increased numerically over the normal content. There were many large clusters of stem cells, although two-thirds of the marrow content consisted of normoblasts. Mitotic figures were abundant and there were moderate numbers of myelocytes and granulocytes.

Summary

A case of aplastic anemia which may have been due to exposure to products of the sulfite pulp industry is reported. It is believed that the toxic substance may have been a benzene derivative present in the exhaust gases. In view of this, it seems important, in the case of patients connected with the sulfite pulp industry, to be on the alert for such symptoms as progressive weakness, loss of weight, pallor, bleeding from the mucous membranes, petechiae, dermatitis and stomatitis, which may be indicative of such poisoning. Minor complaints of these workers are also deserving of a careful examination. Failure to make an early diagnosis in such cases may prove fatal.

This examination should include a thorough cytological study of the blood. It must be remembered, however, that both the clinical manifestations and the blood changes in benzene poisoning may vary markedly in different individuals, and, as pointed out by Hunter,[3] may be quite different from the aplastic anemia shown by the case here reported.

Periodic examination of those exposed to fumes of high concentration and of those handling paper pulp might well be considered, as a means of investigating the industrial hazard involved, as well as protecting the workers.

Conclusions

The case presented is of interest because the development of aplastic anemia may have been caused by constituents of the exhaust gases of the sulfite pulp industry. Further investigation of the effect of cymene, other related terpene derivatives, and other constituents in the exhaust gases, as well as products from other sources in the sulfite pulp industry, may reveal significant effects on the

hematopoietic system. It is clearly understood by the author that the inadequate data in this paper can at best serve only to point the way; much more extended study is indicated.

The author wishes to thank the Mayo Clinic for the necropsy report and laboratory data from the forty-ninth day (table 1).

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EDITORIAL

BRIGHTER BLOOD FOR BLUE BABIES

BRIGHTER blood for blue babies! Yes, and brighter horizons for the anguished parents of these unfortunate youngsters, the majority of whom succumbed from anoxemia or cerebral thrombosis early in childhood after varying periods of chronic invalidism while the medical profession sat helplessly by with nothing to offer along therapeutic lines. Such is the significance of the daring surgical treatment of congenital malformations of the heart in which there is pulmonary stenosis or pulmonary atresia as reported by Blalock and Taussig [1] within the past year.

Prior to November 29, 1944 when the first operation was performed by Blalock on a 15 month old blue baby girl in whom Taussig had established the diagnosis of tetralogy of Fallot with a severe degree of pulmonary stenosis, there had been no satisfactory treatment for pulmonary stenosis or pulmonary atresia. This operation and the studies leading thereto were undertaken with the conviction that, even though the structure of the heart was grossly abnormal, in many instances it might be possible to alter the course of the circulation in such a manner as to lessen the cyanosis and the resultant disability.

It has long been recognized that one of the principal factors in the production of cyanosis in congenital malformations of the heart is the direct shunting of venous blood into the systemic circulation. In their outstanding studies on cyanosis Lundsgaard and Van Slyke [2] showed that there were four important factors in the production of cyanosis: (1) the height of the hemoglobin, (2) the volume of the venous blood shunted into the systemic circulation, (3) the rate of utilization of oxygen by the peripheral tissues, and (4) the extent of aeration of the blood in the lungs. Blalock and Taussig recognized the fact that to induce an increase in the blood flow through the pulmonary circuit should result in an improvement in the oxygenation of the blood with a subsequent decrease in the preëxisting compensatory polycythemia, the cyanosis, and the incapacitating physiological effects of the anoxemia in certain children with congenital heart disease.

The feasibility of anastomosing a systemic artery to one of the pulmonary arteries in experimental animals was demonstrated by Levy and Blalock [3] six years ago. As far as they were aware, this was the first time that both the course and function of a large artery had been altered. Before undertak-

[1] BLALOCK, A., and TAUSSIG, H. B.: The surgical treatment of malformations of the heart in which there is pulmonary stenosis or pulmonary atresia, Jr. Am. Med. Assoc., 1945, cxxviii, 189.

[2] LUNDSGAARD, C., and VAN SLYKE, D. D.: Cyanosis, Medical Monographs, vol. 2, 1923, Williams and Wilkins Company, Baltimore.

[3] LEVY, S. E., and BLALOCK, A.: Experimental observations on the effects of connecting by suture the left main pulmonary artery to the systemic circulation, Jr. Thoracic Surg., 1939, viii, 525.

ing operation on patients, Blalock and his associates performed many experiments in an effort to produce pulmonary stenosis in dogs, but this work met with little success. Finally, in an effort to cause a significant decrease in the oxygen saturation of the arterial blood, one or more lobes of the lungs were removed from each side of the dog's chest and the main arteries and veins of these lobes were connected by end-to-end suture creating bilateral pulmonary arteriovenous fistulas. These procedures resulted in some instances in a pronounced reduction in the oxygen saturation of the arterial blood. As the result of an artificial patent ductus arteriosus made in two such experiments, there was a significant increase in the arterial oxygen saturation. Although this experimentally produced condition was quite different from that seen in patients, it was of interest that the establishment of an anastomosis between systemic and pulmonary arteries caused an increase in the oxygen saturation of the arterial blood despite the fact that several lobes of the lungs had been removed.

Since the "blue baby" operation was devised to compensate for inadequate flow of blood to the lungs, it seemed desirable that the anastomosis be made in such a manner that the blood from the systemic artery would be able to reach both lungs. It was obvious that the suture anastomosis could not be made to the main pulmonary artery because occlusion of this vessel for more than a few minutes causes death. Hence, it appeared that the anastomosis should be made just distal to the division of the main pulmonary artery and that the side of the vessel should be used in order that the blood might flow to both lungs. In brief, the operation consists in the creation of an artificial ductus arteriosus by making an end-to-side anastomosis between a branch of the aorta—either the subclavian or innominate artery—and one of the pulmonary arteries. Because of its larger calibre the innominate artery has proved to be the more satisfactory in children with pronounced anoxemia. The anastomosis of the innominate artery to the pulmonary artery diverts a large volume of blood from the systemic circulation into the pulmonary circulation. By this means, the volume of blood which reaches the lungs for aeration is increased. It follows that a greater volume of oxygenated blood is returned by the pulmonary veins to the left auricle and left ventricle, and consequently a greater volume of oxygenated blood is pumped out into the systemic circulation. Thus the operation enables some blood to bypass the obstruction to the pulmonary circulation.

At the time the original report was submitted for publication, three children, each of whom had a severe degree of anoxemia, had been subjected to this operative procedure. Clinical evidence of improvement was striking and included a pronounced decrease in the intensity of the cyanosis, a decrease in dyspnea, and an increase in tolerance to exercise. In the two cases in which laboratory studies were performed, there was a decline in the erythrocyte count, hemoglobin level and the volume of packed red blood cells, an increase in the oxygen content of the arterial blood, a fall in the oxygen capacity, and—most significant—a decided rise in the oxygen saturation of

the arterial blood. In one child the oxygen saturation rose from 35.5 to 79.7 per cent in nine days, and it reached a value of 83.8 per cent 24 days after operation.

Since the original report was submitted for publication, Blalock [4] has performed the operation on over 70 blue babies. The great majority have been remarkably benefited, the mortality rate has been amazingly low considering the delicacy of the procedure and the poor physical condition of most of the patients, and post-operative complications such as cerebral damage from ischemia following ligation of the common carotid artery have been extremely rare. At the present writing, the conclusion is justified that the operation may be regarded as a God-send to the blue baby.

The types of abnormality which Blalock and Taussig believe should be benefited by this operation are the tetralogy of Fallot (pulmonary stenosis or atresia, dextroposition of the aorta, interventricular septal defect, and right ventricular hypertrophy), pulmonary atresia with or without dextroposition of the aorta and with or without defective development of the right ventricle (all infants with this condition, in whom the spontaneous closure of the ductus arteriosus cuts off the circulation to the lungs, die at an early age), a truncus arteriosus with bronchial arteries, and a single ventricle with a rudimentary outlet chamber in which the pulmonary artery is diminutive in size. The operation is indicated only when there is clinical and radiologic evidence of a decrease in the pulmonary blood flow. The two outstanding features, both of which should be present, are (1) roentgenographic evidence that the pulmonary artery is diminutive in size and (2) clinical and roentgenographic evidence of absence of congestion in the lung fields. The operation should be performed on the right or left side, depending on which vessel is to be used and on which side the aorta descends, since it is important to bear in mind that the occurrence of a right aortic arch is by no means rare in congenital malformations of the heart which give rise to persistent cyanosis. The operation should not be performed when studies reveal a prominent pulmonary conus or pulsations at the hili of the lungs. It is not indicated in cases of complete transposition of the great vessels or in the so-called "tetralogy of Fallot of the Eisenmenger type," and probably not in aortic atresia. When one considers the many variations in the anatomy of the heart and great vessels which may be encountered in patients with congenital heart disease, it becomes all the more apparent how essential a pediatric cardiologist such as Taussig, who has devoted so much of her life to the study and recognition of these anomalies, must be both for the selection of candidates for surgical therapy and for the decision as to which side of the thorax should best be explored.

So much then for the new and revolutionary surgical treatment of certain forms of congenital heart disease. It is too early to predict what the late results of this radical form of therapy may be. Will these patients

[4] BLALOCK, A.: Personal communication.

eventually succumb to heart failure, will the incidence of bacterial endocarditis be unusually high, or, from the eugenic angle, will these surgically "rouged" blue babies grow up to procreate more of their kind? These are questions that must be left to the future. The immediate results have been nothing short of brilliant, and the medical profession—not to mention the blue babies—may well bow in admiration to the foresighted surgeon and pediatrician who have collaborated so effectively to alleviate one of the most distressing conditions that may afflict an innocent babe.

W. H. B.

REVIEWS

Handbook of Physiology and Biochemistry. By R. J. S. McDowall, M.D., D.Sc., M.R.C.P. 898 Pages; 21 × 15 cm. 1945. The Blakiston Company, Philadelphia. Price, $6.00.

Originally "Kirke's" and later "Haliburton's." The textbook undoubtedly suffers from the inclusion of too much material about which the author has only limited knowledge. Some of the biochemical presentations are vague and misleading so that even one familiar with the subject has difficulty following the thought.

Other material has not been brought up to date. For example, the classical B oxidation of fatty acids is presented without any indication of the newer concepts of fat oxidation. This tendency is frequently evident. The discussion of the Rh factor is unsatisfactory.

Many will not agree with the sentiments of the author who justifies his choice of material by saying in the preface "—and it will do no harm if the student catches a fleeting glance of things he need not know, for soon he will realize that his knowledge of medicine generally must of necessity be most patchy and superficial."

M. A. A.

BOOKS RECEIVED

Books received during December are acknowledged in the following section. As far as practicable, those of special interest will be selected for review later, but it is not possible to discuss all of them.

The Tissues of the Body. An Introduction to the Study of Anatomy. Second Edition. By W. E. Le Gros Clark, F.R.S. 388 pages; 24.5 × 16.5 cm. 1945. The Oxford University Press, New York City.

A Future for Preventive Medicine. By Edward J. Stieglitz, M.D., F.A.C.P. 77 pages; 22 × 14 cm. 1945. The Commonwealth Fund, New York City. Price, $1.00.

The Physician's Business. Second Edition. By George D. Wolf, M.D. Foreword by Harold Rypins, A.B., M.D., F.A.C.P. 433 pages; 23.5 × 15.5 cm. 1945. J. B. Lippincott Company, Philadelphia. Price, $6.00.

An Introduction to Physical Anthropology. By M. F. Ashley Montagu, Associate Professor of Anatomy, Hahnemann Medical College and Hospital, Philadelphia. Visiting Lecturer, Department of Sociology, Harvard University. 325 pages; 21.5 × 14.5 cm. 1945. Charles C. Thomas, Springfield, Illinois. Price, $4.00.

Manual of Diagnosis and Management of Peripheral Nerve Injuries. By Robert A. Groff, M.D., Lt. Col., M.C., A.U.S., and Sara Jane Houtz, B.S., First Lieutenant (P.T.), A.U.S. With an Introduction by I. S. Ravdin, M.D. 188 pages; 23.5 × 16 cm. 1945. J. B. Lippincott Company, Philadelphia. Price, $8.00.

Ninth Service Command—Conference on Internal Medicine. Held at Letterman General Hospital—November 7–8, 1945. 106 pages; 27 × 20.5 cm. 1945.

COLLEGE NEWS NOTES

A.C.P. Postgraduate Courses

Spring Bulletin of Postgraduate Courses Authorized by the Advisory Committee on Postgraduate Courses, the Committee on Educational Policy, and the Board of Regents

As in the past the College will again sponsor a series of intensive, advanced short postgraduate courses which will be held at various medical schools and university teaching hospitals throughout the country, in the spring of 1946 and again in the autumn. These courses have been arranged through the generous coöperation of the directors and the institutions at which the courses will be given.

The courses are organized especially for Fellows and Associates of the College, but where facilities are available, they will be open to non-members with adequate preliminary training, preference to be given to non-members in the following order: (1) candidates for membership; (2) Medical Officers in the Armed Forces; (3) physicians preparing for examinations by their certifying boards; (4) other non-members having adequate background for advanced work. By direction of the Board of Regents registrations from non-members of the College may not be accepted more than three weeks in advance of the opening of any course.

The courses are made available by the College to its members at minimum cost, because the College assumes full responsibility for promotion, advertising, printing and registration.

Fees. $20.00 per week to members of the College; $40.00 per week to non-members; Medical Officers of the Armed Forces of the United States and Canada, free. For purely clinical courses where the instruction must be more personalized and individualized for groups of 12 or less, the fees shall be $40.00 and $80.00 to A.C.P. members and non-members, respectively.

Detailed bulletin of courses and registration forms are available through Dr. C. C. Shaw, Educational Director, 4200 Pine St., Philadelphia, 4, Pa.

Course No. 1—Clinical Allergy (March 4–9; April 8–13; July 8–13)
Massachusetts General Hospital, Boston, Mass.
Francis M. Rackemann, M.D., F.A.C.P., Director
(Registration, 6 men only, each week)
Fee: A.C.P. Members, $40.00 per week; Non-Members, $80.00 per week; Medical Officers on Active Duty or Terminal Leave, No Charge.

This is an advanced course in Clinical Allergy which is designed for those men who already have some knowledge of the subject and who wish an opportunity to discuss the new advances and the current problems.

The registrants will see and discuss with Dr. Rackemann and his associates the management of patients in the Clinic and in the wards at the Massachusetts General Hospital. Afternoons will be devoted in rotation to methods and problems in the laboratory, to special reading, and to observations of patients and problems in the private office.

Registration will therefore be limited to six men in March, to another six in April, and to a third group of six only during the proposed week in July.

Course No. 2—General Medicine (March 18–23, 1946)
Jefferson Medical College, Philadelphia, Pa.
Hobart A. Reimann, M.D., F.A.C.P., Director

(Minimal Registration, 75; Maximal Registration, 100)
Fee: A.C.P. Members, $20.00; Non-Members, $40.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

An intensive course in General and Internal Medicine will be offered by the faculty of the Jefferson Medical College under the Directorship of the Professor of Medicine, Dr. Hobart A. Reimann.

Recent advances in diagnosis and therapy accruing during the war years will be thoroughly presented in an informal style. The majority of the sessions will be held in the Amphitheatre of the Jefferson Hospital, Philadelphia, where illustrative clinical cases will be presented, films and slides shown and clinical pathological conferences will be held.

Course No. 3—General Medicine (March 25–30, 1946)
University of Texas—School of Medicine, Galveston, Texas
CHARLES T. STONE, M.D., F.A.C.P., Director
(Minimal Registration, 25; Maximal Registration, 50)
Fee: A.C.P. Members, $20.00; Non-Members, $40.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

A review course in General Medicine will be offered at the University of Texas School of Medicine in Galveston from March 25 to 30, 1946, under the Directorship of Dr. Charles T. Stone, Professor of Medicine. A detailed outline of the course has not yet been received, but registrants will be provided with excellent and valuable instruction in the practical aspects of general medical practice as well as in diagnosis and therapy of Tropical Diseases in the light of modern advances in this field during the recent global conflict.

Clinics and demonstrations will be held at the John Sealy Hospital and associated institutions in Galveston.

Course No. 4—Internal Medicine (April 1–19, 1946)
Massachusetts General Hospital, Boston, Mass.
JAMES H. MEANS, M.D., F.A.C.P., Director
(Minimal Registration, 60; Maximal Registration, 80)
Fee: A.C.P. Members, $60.00; Non-Members, $120.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

A general course in the principles and practice of Internal Medicine will be given at the Massachusetts General Hospital under the directorship of Dr. J. H. Means, who is Jackson Professor of Clinical Medicine at the Harvard Medical School and Chief of Medical Services of the Massachusetts General Hospital.

This proposed course will stress the fundamentals of Internal Medicine.

Various members of the Harvard Medical School faculty, who are serving in other Boston hospitals and institutions, will be invited to participate in the presentations.

Course No. 5—Metabolism and Nutrition (June 3–8, 1946)
Nutrition Clinic, Hillman Hospital, Birmingham, Alabama
TOM D. SPIES, M.D., F.A.C.P., Director
(Minimal Registration, 10; Maximal Registration, 15)
Fee: A.C.P. Members, $40.00; Non-Members, $80.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

An intensive personalized course in Metabolism and Nutrition will be directed by Tom D. Spies at the Nutrition Clinic of the Hillman Hospital in Birmingham, Alabama, for a small group of from 10 to 15 men. The course will be devoted to the

various phases of nutrition and nutritional deficiencies in a practical and stimulating manner, including clinics and ward rounds, field studies, and laboratory demonstrations. Deficiency producing diets and therapeutic diets will be stressed. The principles of nutrition and metabolism will be defined, and the diagnosis and treatment of deficiency states will be presented by means of informal discussions and clinics. Nutrition in relation to dentistry, heart failure, and public health will be presented.

Dr. Tom Spies will be assisted by his associates and colleagues from the Medical College of Alabama and the University of Cincinnati College of Medicine.

Course No. 6—General Medicine (April 22–27, 1946)
Emory University School of Medicine, Atlanta, Georgia
James E. Paullin, M.D., F.A.C.P., Director
(Minimal Registration, 15; Maximal Registration, 25)
Fee: A.C.P. Members, $20.00; Non-Members, $40.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

Under the directorship of Dr. James E. Paullin, an intensive course covering most of the fields of General Medicine will be presented in Atlanta from April 22 to 27, 1946.

The faculty of Emory University Medical School will serve under the leadership of Dr. Eugene A. Stead, Jr., Professor of Medicine.

Clinical instruction of a high order will be provided at the following hospitals: Piedmont, Grady, Emory University and Georgia Baptist Hospitals.

Atlanta is even more beautiful in the spring.

Course No. 7—Gastro-Enterology (April 29–May 4, 1946)
Graduate Hospital, Philadelphia, Pa.
Henry L. Bockus, M.D., F.A.C.P., Director
(Minimal Registration, 50; Maximal Registration, 100)
Fee: A.C.P. Members, $20.00; Non-Members, $40.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

A course in Gastro-enterology has been scheduled in Philadelphia from April 29 to May 4, 1946.

Sessions will be held at the Graduate Hospital of the University of Pennsylvania under the Directorship of Dr. Henry L. Bockus. Previous courses sponsored by this group have provided instruction of a high order in this sub-specialty.

Course No. 8—Cardiology (May 6–11, 1946)
Philadelphia General Hospital and the Woman's Medical College of Pennsylvania, Philadelphia, Pa.
William G. Leaman, Jr., M.D., F.A.C.P., Director
(Minimal Registration, 75; Maximal Registration, 100)
Fee: A.C.P. Members, $20.00; Non-Members, $40.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

A course in Cardiology will be given in Philadelphia, Pa., by a composite faculty, under the Directorship of Dr. William G. Leaman, Jr., who is Professor of Medicine of the Woman's Medical College of Pennsylvania.

Sessions will be held during the day at the Philadelphia General Hospital. In the evening, an interesting and rather unusual program, devoted to the basic sciences and their relation to Cardiology, will be given by the members of the preclinical faculty of the Woman's Medical College. Among members of the faculty who will participate are: James O. Brown, Ph.D., Associate Professor and Acting Head of the Department of Anatomy; Mollie A. Geiss, M.D., Professor of Pathology; Lloyd

D. Seager, M.D., Professor of Pharmacology and Toxicology; Roberta Hafkesbring, Ph.D., Professor of Physiology.

Recent advances in anatomy, physiology, pharmacology, and pathology in their relation to cardiac problems will be presented. This program promises information valuable to the general internist as well as to the cardiologist.

Incidentally, this course directly precedes the Annual Session of the College, to be held in Philadelphia from May 13 to 17, inclusive.

Course No. 9—Chest Diseases (May 6–11, 1946)

University of Michigan, Medical School and Hospital, Ann Arbor, Michigan

JOHN ALEXANDER, M.D., F.A.C.S., Director

(Minimal Registration, 25; Maximal Registration, 50)

Fee: A.C.P. Members, $20.00; Non-Members, $40.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

This will be an excellent course in Diseases of the Chest, under the Directorship of Dr. John Alexander. The staff of the University of Michigan Medical School and Hospital will participate in the presentations, and it is believed that registrants will find this seminar both highly interesting and instructive.

The treatment of wounds and chest conditions resulting from combat and exposure will be emphasized in the light of newer technic and chemotherapeutics developed during the recent global conflict.

This course will be of extraordinary value to internists and specialists as well as to medical officers and civilian physicians.

Course No. 10—Internal Medicine (June 17–28, 1946)

University of California, Medical School and Medical Center San Francisco, California

STACY R. METTIER, M.D., F.A.C.P., Director

(Minimal Registration, 20; Maximal Registration, 40)

Fee: A.C.P. Members, $40.00; Non-Members, $80.00; Medical Officers on Active Duty or Terminal Leave, No Charge.

Dr. Stacy R. Mettier, Professor of Medicine and Chairman of the Committee on Postgraduate Instruction of the University of California Medical School, will direct a course in Internal Medicine for the College in San Francisco from June 3 to 14, inclusive.

The University of California offers superior facilities, an outstanding faculty and inspiring surroundings for this course, which will precede the Annual Convention of the American Medical Association in San Francisco.

A final Bulletin of Spring Courses, containing complete descriptions, outlines of courses, faculty personnel, living accommodations, etc., will be published soon and mailed to all members of the College and to non-members who have requested entry of their names on the mailing list.

Arrangements for living accommodations are being concluded; names of hotels and room rates will be published in the final Bulletin. Because of generally crowded conditions throughout the country, it has become very difficult to obtain reservations for single rooms. Most hotels can provide only double rooms with twin beds, which will necessitate doubling up by our registrants for these courses. Please inform the hotel, where you plan to reside, with whom you are willing to share a room.

Autumn Courses, 1946—A number of varied and interesting courses are being arranged for the autumn. Further announcements concerning the development of our educational program will appear in ensuing issues of the ANNALS OF INTERNAL MEDICINE.

Members who are interested in discussing the educational program of our college are invited to write to, or consult with, the Educational Director, C. C. Shaw, M.D.

27TH ANNUAL SESSION OF THE COLLEGE, PHILADELPHIA, PA., MAY 13–17, 1946

The 27th Annual Session of the American College of Physicians will be held in Philadelphia, Pa., from May 13 to May 17, inclusive, 1946. Hotel headquarters will be at the Benjamin Franklin Hotel. The general sessions and the exhibits will be located in the Philadelphia Convention Hall, located at 34th Street below Spruce, opposite the Philadelphia General Hospital.

Registration will begin Monday morning at 9 o'clock in the Convention Hall, and the remainder of that morning is unscheduled to allow registrants a chance to familiarize themselves with the technical exhibits.

The first General Session will be held at 2:00 p.m. on Monday, May 13. A General Session will be held each afternoon, Monday through Friday. On Thursday afternoon at 4 p.m. the Annual Business Meeting of the College will be held, directly after the end of the 4th General Session. All Fellows of the College are urged to be present to hear the annual reports of the Officers, to vote in the election of Officers, Regents, and Governors of the College, and to see the President-Elect, Dr. David P. Barr, of New York, inducted into the office of President of the College.

The retiring President, Dr. Ernest E. Irons, of Chicago, is in charge of the program of General Sessions and of Special Lectures. In addition, he is responsible for the program of the Victory Convocation, which will be held Wednesday evening, May 15, at the Benjamin Franklin Hotel, and will be followed by the President's reception to newly inducted Fellows of the College.

Dr. George Morris Piersol, of Philadelphia, has been appointed General Chairman of the Session, and his duties include appointment of Committees, to make local arrangements for the clinic program, the panel program, and the entertainment features, culminating in the Annual Banquet of the College to be held at the Benjamin Franklin Hotel on Thursday evening, May 16.

Arrangements for the clinical aspects of the Session are now well under way. All the outstanding local hospitals have agreed to contribute to our program. Members of the hospital and teaching staffs will present numerous and varied clinics, including ward walks for limited groups, case presentations, and clinical pathological conferences. The Committee on Clinics and the Hospitals participating are as follows:

Dr. Thomas Fitz-Hugh, Jr., F.A.C.P., Chairman
University of Pennsylvania Hospital—Dr. T. Grier Miller, F.A.C.P.
Jefferson Hospital—Dr. Hobart A. Reimann, F.A.C.P.
Temple University Hospital—Dr. Charles L. Brown, F.A.C.P.
Pennsylvania Hospital—Dr. David Cooper, F.A.C.P.
Graduate Hospital—Dr. Henry L. Bockus, F.A.C.P.
Children's Hospital—Dr. Joseph Stokes
Institute of the Pennsylvania Hospital—Dr. Kenneth E. Appel, F.A.C.P.
Lankenau Hospital—Dr. Edward L. Bortz, F.A.C.P.
Presbyterian Hospital—Dr. Joseph T. Beardwood, Jr., F.A.C.P.
Hahnemann Hospital—Dr. G. Harlan Wells, F.A.C.P.
Woman's Medical College—Dr. William G. Leaman, Jr., F.A.C.P.
Jewish Hospital—Dr. Joseph C. Doane, F.A.C.P.
Philadelphia General Hospital—Dr. Truman G. Schnabel, F.A.C.P.
U. S. Naval Hospital—Captain Walter H. Schwartz, MC, USN

It will be noted that the morning hours may be devoted either to hospital clinics at the various Philadelphia institutions or to a series of scientific lectures of sufficient length to allow the lecturer to cover thoroughly recent advances in his subject by means of lantern slides, graphic charts, moving picture films, and/or other demonstrations. These morning lectures will be held in the Convention Hall from 9:30 to 11:30, and will be followed by panel discussions of outstanding clinical problems by authorities in the various subjects from 12 noon until 1:15 p.m.

A cafeteria in the Convention Hall will provide luncheon from 1:15 to 2:15 p.m. The General Sessions will take up the remaining portion of the afternoon schedule.

No scientific sessions will be held in the evening.

On Sunday evening, May 12, the Annual Dinner and combined meeting of the Board of Regents and the Board of Governors will take place in the Benjamin Franklin Hotel. The Entertainment Committee promises a delightful and stimulating evening and opening reception on Monday, May 13, from 8 p.m. to 11 p.m. This will probably be held in the Ball Room of the Benjamin Franklin Hotel.

Tuesday evening, May 14, has no official schedule. The date has purposely been left open to provide an opportunity for private dinners, cocktail parties, and theater groups.

On Wednesday evening, May 15, the great Victory Convocation will be held in the Grand Ball Room of the Benjamin Franklin Hotel, where Fellowships will be conferred on those physicians who have qualified for this honor since the outbreak of the war. This is a very important function of the College, and the ceremony should be not only impressive but epic making in the history of our society. The John Phillips Memorial Medal will be awarded to an outstanding scientist. A full attendance is urged, as our retiring President, Dr. Ernest E. Irons, will address us. All present are invited to the President's reception, with dancing, which immediately follows the Victory Convocation.

The Annual Banquet of the College on Thursday evening, May 16, will complete the list of social functions at this 27th Annual Session. The Committee on Arrangements has promised a gala affair which will contribute to the high order of our program and provide a fitting social finale to your Philadelphia visit.

New Life Members

The following Fellows of the College have become Life Members: (Listed in the order of subscription.)

Dr. Albert T. Leatherbarrow, Hampton Station, N.B., Canada
Dr. William M. LeFevre, Muskegon, Mich.
Dr. Allen H. Bunce, Atlanta, Ga.
Dr. George H. Anderson, Spokane, Wash.
Dr. David B. Flavan, St. Louis, Mo.
Dr. David W. Kramer, Philadelphia, Pa.
Dr. Charles T. Stone, Galveston, Tex.
Comdr. O. V. Calhoun, (MC), USNR, Lincoln, Nebr.
Dr. Harold W. Gregg, Butte, Mont.
Dr. William W. Alexander, Florence, Ala.
Dr. Jacob S. Blumenthal, Minneapolis, Minn.
Dr. George Tryon Harding, III, Columbus, Ohio.
Dr. Frank G. LeFor, Yakima, Wash.

Gifts to the College Library

The following gifts of publications by members are gratefully acknowledged:

Coy C. Carpenter, F.A.C.P., Winston-Salem, N. C.—1 reprint
Henry B. Gwynn, F.A.C.P., Washington, D. C.—1 reprint
Paul J. Hanzlik, F.A.C.P., San Francisco, Calif.—4 reprints
Samuel I. Kooperstein, F.A.C.P., Jersey City, N. J.—1 reprint
Louis S. Lipschutz, F.A.C.P., Eloise, Mich.—1 reprint
Harry R. Litchfield, F.A.C.P., Brooklyn, N. Y.—1 reprint
George W. Parson, F.A.C.P., Texarkana, Tex.—2 reprints
Michael Peters, (Associate), Fort Benning, Ga.—2 reprints
Lawrence E. Putnam, (Associate), Washington, D. C.—1 reprint
Michael W. Shutkin, F.A.C.P., Milwaukee, Wis.—1 reprint
George E. Baker, F.A.C.P., Casper, Wyoming—4 reprints
Robert C. Page, F.A.C.P., White Plains, N. Y.—12 reprints

The College Headquarters acknowledges with thanks the gift of the publisher, Instituto Nacional de Cardiologia, copy No. 74 of "Libro Homenaje al Doctor Ignacio Chavez." This volume is a biographical sketch of the career of Dr. Chavez, who is a distinguished Fellow of the American College of Physicians. The volume has been added to our College library.

Lt. Col. Henry B. Gwynn, of Washington, D. C. entered active service on May 14, 1942, and was promoted to the rank of Major on May 2, 1943, and to Lieutenant Colonel on January 1, 1946.

Dr. Manfred Kraemer, F.A.C.P., of Newark, New Jersey, was promoted to the grade of Lieutenant Colonel as of November 17, 1945, and was released to inactive duty (his terminal leave ending January 21, 1946) with this rank, to resume his private practice.

Surgeon General Kirk of the United States Army, in a Bulletin emanating from the Office of the Surgeon General, Technical Information Division, describes in detail the advantages of Army careers for doctors. An extensive program of graduate medical education and research for Medical Corps officers has been established which will attract the interest of younger internists and those who are seeking qualification by the Specializing Boards. Army fellowships, residencies and special courses are in operation to further this program designed to aid in advancing the personnel of the Medical Department from a professional standpoint.

Under a new law, any doctor, physically and professionally qualified, who has been on active duty in the Army since Pearl Harbor, and who is under forty-five years of age, is eligible for appointment in the Regular Army, unless he has been separated from the service under other than honorable conditions.

His grade will be determined by his age, within limits, or his length of service as a commissioned officer in the Army, whichever is the greater factor. Commissions will encompass the ranks of First Lieutenant, Captain and Major.

The opportunities outlined above are also available to officers in the Pharmacy and the Sanitary Corps and also in the Medical Administrative Corps. Application blanks may be obtained at any Army installation or unit headquarters or upon written request to the Adjutant General's Office, War Department, Washington 25, D. C. Applications must reach the Adjutant General's Office not later than March 10, 1946.

Fellowships in Medical Research

The National Research Council is offering fellowships in the fields of cancer research and anesthesiology to veteran medical officers returning to civilian life from the Armed Forces. These fellowships are intended for men, as a rule, under thirty-four years of age, and are scheduled for a period of one year of research. Application forms may be obtained from the Chairman, Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

Refresher Training for Doctors Leaving Service

According to News Notes, No. 35, of December 31, from the Technical Information Division, Office of the Surgeon General, refresher training of 12 weeks' duration will be given Army doctors leaving the service who desire to brush up on latest developments in fields of medicine, surgery, or neuropsychiatry in which they may not have been actively practicing during the past year.

This training, which will prepare retiring Army doctors for return to private practice with latest knowledge of medical advances made during the war, will be given at Army hospitals until June 30, 1946. Reserve Corps, National Guard, and AUS Medical Corps officers who are to be separated will be eligible for this schooling.

Lt. Col. Henry B. Gwynn, MC, AUS, F.A.C.P., has been appointed Director of the Reconditioning Consultants Division, Office of the Surgeon General.

Thomas Parran, M.D., F.A.C.P., Surgeon General of the U.S. Public Health Service, states that there are 900 vacant full-time positions in state and local health departments. Half of these vacancies are being held for individuals on leave in the military service. The other half are vacancies without restrictions waiting to be filled by qualified physicians.

Captain Forrest M. Harrison, MC, USN, F.A.C.P., has been appointed Director of the Psychiatric Personnel Placement Service, which is designed to aid physicians and psychiatrists in making contact with training opportunities, such as residencies, postgraduate courses, fellowships, and desirable institutional appointments.

This newly established Psychiatric Personnel Placement Service is sponsored jointly by the American Psychiatric Association and the National Committee for Mental Hygiene.

Inquiries should be addressed to Captain Forrest M. Harrison, MC, USN, National Committee for Mental Hygiene, 1790 Broadway, New York City 19.

Colonel John R. McBride, MC, AUS, F.A.C.P., has been appointed an Associate in Medicine at the Peter Bent Brigham Hospital to work under the direction of Dr. George W. Thorn, F.A.C.P.

Lieutenant Colonel Louis S. Lipschutz, MC, AUS, F.A.C.P., has been appointed Medical Director (Psychiatric) of the Wayne County General Hospital, Eloise, Michigan.

Dr. George X. Schwemlein, F.A.C.P., Co-Director of the Chicago Intensive Treatment Center and Passed Assistant Surgeon (Reserve), United States Public

Health Service, addressed a combined meeting of the Cincinnati Academy of Medicine, Health Department and Dermatological Society on October 16, 1945, on the subject, "The Present Status of Penicillin in the Therapy of Syphilis."

Colonel William B. Meister, MC, USA, has been appointed Superintendent of the St. Luke's Hospital in Newburgh, New York.

Dr. Edward L. Bortz, F.A.C.P., of Philadelphia, who was recently discharged from military service with the rank of Captain in the Medical Corps of the U.S. Naval Reserve, discussed "Implications of the Atomic Bomb" before the North Side Branch of the Chicago Medical Society, December 6, 1945, in the Drake Hotel.

Dr. George W. McCoy, F.A.C.P., Professor and Director of the Department of Public Health, Louisiana State University School of Medicine, New Orleans, has been appointed Acting Dean.

Dr. Clement C. Fenton, F.A.C.P., Professor and Head of the Department of Pathology of the West Virginia University School of Medicine, Morgantown, West Virginia, has been elected President of the newly organized Association of Pathologists of West Virginia.

Dr. Theodore G. Klumpp, F.A.C.P., of New York City, is checking on clinical experiments using organic antimony compounds in the treatment of filariasis, at the School of Tropical Medicine, San Jaun, Puerto Rico.

Tulane University School of Medicine, New Orleans, Louisiana, has received a bequest in the amount of $1,075,000 for endowment of the Chair of Tropical Medicine.

The New York State Department of Health has available a limited number of Fellowships for veteran medical officers who wish to devote their careers to the practice of civilian public health on a full time basis. Fellowship provisions are generous and include tuition for study at a postgraduate school of public health leading to a master's degree. Additional information and application blanks may be obtained from the New York State Department of Health, Albany 1, New York.

Colonel Eugene C. Eppinger, MC, AUS, F.A.C.P., has been appointed Assistant Dean in charge of courses for graduates at the Harvard Medical School, Boston. Colonel Eppinger will have charge of the direction of all courses for graduates, including the refresher courses for returning veterans. Initial plans for this postgraduate program have been drawn up by the Committee, under the direction of Dr. Chester M. Jones, F.A.C.P., of Boston.

Dr. Oscar A. Sander, F.A.C.P., of Milwaukee, Wis., participated in the presentation of a course in Occupational Health and Medicine at the Wayne University School of Occupational Health, which sponsored a twelve week orientation course in this field, beginning January 7.

Dr. Lillian L. Nye, F.A.C.P., formerly of St. Paul, Minn., has been appointed head of the Health Service of the Mississippi State College for Women at Columbus.

Dr. Felix J. Underwood, F.A.C.P., of Jackson, Miss., who is Executive Officer of the Mississippi State Board of Health, was appointed by Governor Thomas L. Bailey on September 24, 1945, a member of the Mississippi Children's Code Commission.

Dr. Cornelius P. Rhoads, F.A.C.P., of New York City, delivered the seventh annual Barnard Hospital Lecture before the St. Louis Medical Society on November 20, 1945. Dr. Rhoads discussed the "Nutritional Aspects of the Cancer Problem."

Dr. S. Douglas Craig, F.A.C.P., Winston-Salem, North Carolina, President of the North Carolina State Board of Health, has been named to direct the Surplus Properties program in that state, serving as the liaison officer between the hospitals and public health agencies in matters affecting surplus Government properties.

Dr. George R. Minot, F.A.C.P., of Boston, Mass., was honored at a dinner on December 5, 1945, in recognition of his outstanding achievements in medicine and in honor of his sixtieth birthday which he observed December 2. Dr. William B. Castle, F.A.C.P., served as toastmaster, and the speakers included Dr. Henry A. Christian, F.A.C.P., Brookline; Dr. Charles Sidney Burwell, F.A.C.P., Dr. Elliott P. Joslin, F.A.C.P., Dr. James Howard Means, F.A.C.P., and Dr. Francis M. Rackemann, F.A.C.P., all of Boston.

Dr. Reginald Fitz, F.A.C.P., of Boston, representing the President and the House of Delegates of the American Medical Association, presented to Dr. Minot its Distinguished Service Medal for his achievements.

Dr. Joseph T. Roberts, (Associate), of Washington, D.C., was chosen the Davidson Lecturer of the Medical Society of the District of Columbia in 1945. Dr. Roberts, Adjunct Clinical Professor of Medicine at Georgetown University School of Medicine, submitted a paper on "The Rôle of the Small Vessels and Nerves of the Heart in Heart Failure and Cardiac Pain."

Dr. William F. O'Donnell, F.A.C.P., of the Georgetown University School of Medicine, Washington, was promoted to the rank of Professor and Acting Director of the Department of Pediatrics.

Dr. Richard Hugh Wood, F.A.C.P., of Atlanta, Ga., has been appointed Associate Professor of Medicine at Emory University Medical School and Physician-in-Chief at Emory University Hospital.

Dr. Charles L. Hess, F.A.C.P., of Bay City, Mich., has been reappointed a member of the State Advisory Committee for Vocational Rehabilitation, representing the Michigan State Medical Society.

Dr. Raymond Hussey, F.A.C.P., of Detroit, representing Wayne University, is a member of the Rehabilitation Advisory Committee.

The following Fellows of the American College of Physicians were elected to officership in the Institute of Medicine of Chicago by the Board of Governors on December 12, 1945: Dr. Ernest E. Irons, President of the Institute; Dr. George H. Coleman, Secretary; and Dr. Grant H. Laing, Treasurer. Dr. Italo F. Volini, F.A.C.P., was elected to membership on the Board of Governors for a term of five years.

Dr. Jay Arthur Myers, F.A.C.P., Minneapolis, Minn., who has been Professor of Preventive Medicine and Public Health, Division of Public Health Administration and Epidemiology, University of Minnesota Medical School, has been elected Editor-in-Chief of the *Journal of the American College of Chest Physicians.*

Dr. Wann Langston, F.A.C.P., Professor of Medicine and Chairman of the Department of Medicine at the University of Oklahoma School of Medicine, Oklahoma City, has been appointed Acting Dean of the school.

Dr. Samuel M. Feinberg, F.A.C.P., of Chicago, and Dr. Robert A. Cooke, F.A.C.P., of New York, presented papers at the seminar of the American Academy of Allergy recently at the New York Postgraduate Medical School.

A Research Fund sponsored by the American Life Convention and the Life Insurance Association of America for grants to support fundamental research in cardiovascular disease and allied disorders, has been created through the coöperation of one hundred and forty-six life insurance companies in the United States and Canada by establishing the Life Insurance Medical Research Fund.

Dr. Francis G. Blake, F.A.C.P., of New Haven, was named Chairman of the Advisory Council of eight members, among whom are the following Fellows of the American College of Physicians: Dr. Eugene M. Landis, Boston; Dr. Robert F. Loeb, New York; Dr. Seeley G. Mudd, Los Angeles; and Dr. Cecil J. Watson, of Minneapolis; which council will assist the board of directors of this fund in making grants. Application blanks may be obtained from Dr. Blake's office at Yale University School of Medicine, New Haven 11, Conn. Applications must be transmitted in duplicate through the administrative officer of the institution making application.

Dr. Karl Figley, F.A.C.P., Toledo, Ohio, has been elected a member of the temporary Executive Committee of the International Association of Allergists. Plans are under way to hold the First International Congress in Paris in 1948. The first Pan American Congress of the American College of Allergists is planned for Oakland, Calif., June 28–30.

The American Gastroenterological Association will hold its annual meeting at the Hotel Claridge, Atlantic City, May 24–25. Dr. Jacob Arnold Bargen, F.A.C.P., Rochester, Minn., is Secretary.

The Aero Medical Association of the United States will hold its annual convention at the Edgewater Beach Hotel, Chicago, April 7–9.

The American Public Health Association has announced that it will hold its 74th annual meeting at Cleveland either during the week of November 11 or November 18, 1946. Further announcements will follow.

SCHEDULE OF ORAL EXAMINATIONS—1946

AMERICAN BOARD OF INTERNAL MEDICINE

1 West Main Street
Madison 3, Wisconsin

	Date Oral Exam.	Closing Date for Filing Application	For Candidates Residing in the Following States			
Philadelphia Pa.	May 9–10–11 1946	March 15, 1946	New Hamp. Maine Vermont Mass.	Conn. New York Penna. New Jersey	Maryland Rhode Is. West Va. Virginia No. Carolina	So. Carolina Georgia Florida Dist. of Col. Delaware
San Francisco Calif.	June 27–28–29 1946	April 15, 1946	Montana Idaho	Utah Washington	Oregon Nevada	California Wyoming

The above schedule will be sufficiently flexible to accept eligible candidates who are in the service and have a change of station before the examination.

The Board will appreciate your kind consideration in not requesting admission unless you are reasonably sure of being present. The difficulty of transportation and late trains may interfere with an efficient schedule. It is hoped, however, that all candidates will be able to obtain train and hotel accommodations.

The Board will find it difficult to accept applications after the closing date except for officers who have just returned from overseas and have been unaware of the closing dates.

The Committee on Credentials will meet at the College Headquarters in Philadelphia about the middle of April and again on May 12, 1946. No more meetings of this Committee will be held thereafter until the late autumn of 1946. All proposals for membership and advancement to Fellowship must be filed with the Committee on Credentials thirty days prior to any meeting of this Committee.

Candidates for admission to the College who reside in Eastern Pennsylvania must be endorsed by Dr. Edward L. Bortz, of Philadelphia, who is Governor for this district.

Candidates residing in Michigan must be endorsed by the Governor for Michigan, Dr. Douglas Donald, of Detroit.

Candidates for membership who are practicing in the State of Washington must be endorsed by Dr. Charles E. Watts, of Seattle.

The Board of Regents and the Officers of the College are grateful to Dr. Thomas M. McMillan, Dr. Patrick L. Ledwidge, and Dr. Edwin G. Bannick, who served as Acting Governors of these areas during the leave of absence of the appointed Governors on military duty.

Because of the volume of applications for Clinical Fellowships in Medicine, it was found necessary to establish a closing date for filing applications as of February 1, 1946.

Funds are available for one or two additional Research Fellowships. Applications will be accepted until April 1, 1946. Blank forms may be obtained from the office of the Educational Director, 4200 Pine Street, Philadelphia 4, Pa.

Dr. LeRoy B. Duggan, F.A.C.P., has been retired from active duty in the United States Naval Reserve and is now located in the Medical Arts Building, Houston, Texas. He is Visiting Physician at the Jeff Davis Hospital, Internist at the Hermann Hospital, Consulting Internist at the Southern Pacific Hospital, and Associate Professor of Clinical Medicine at Baylor University College of Medicine.

Dr. Lorenz M. Waller who is on terminal leave from the Medical Corps of the Army has resumed his work as Senior Physician on the Attending Staff of the Los Angeles County Hospital and on the Attending Staff of the Hollywood Presbyterian Hospital. He is on the Associate Staff of the Queen of Angels Hospital also. His office is at 1680 N. Vine Street, Hollywood.

Dr. Joseph B. Cady, following his discharge recently from the Army, is now in charge of the Section of Cardiology and Thoracic Medicine at the Guthrie Clinic of the Robert Packer Hospital, Sayre, Pennsylvania. Before the war Dr. Cady was located in Lebanon, Pennsylvania.

Dr. D. Sergeant Pepper, F.A.C.P., Philadelphia, Pa., following separation from the Medical Corps of the Army as Lieutenant Colonel, has accepted a full time appointment in the medical department of the Provident Mutual Life Insurance Company of Philadelphia.

Dr. James Roby Gudger, F.A.C.P., formerly of West Hartford, Conn., has retired from active duty in the Naval Reserve, and on January 2, 1946, assumed the office of Medical Director of the Mutual Life Insurance Company of New York, with headquarters at 34 Nassau St., New York City.

Retirements from Military Service

Since the last publication of this journal the following members of the College have been reported retired or on terminal leave:

Leonard M. Asher, Los Angeles, Calif. (Major, MC, AUS)
Noyes L. Avery, Jr., Grand Rapids, Mich. (Major, MC, AUS)
John A. Baird, Fargo, N. D. (Major, MC, AUS)
Louis J. Benton, Ogdensburg, N. Y. (Capt., MC, AUS)
Reuben Berman, Minneapolis, Minn. (Lt. Col., MC, AUS)
Maxwell G. Berry, Kansas City, Mo. (Lt. Col., MC, AUS)
Philip B. Bleecker, Memphis, Tenn. (Major, MC, AUS)
Franklin B. Bogart, Chattanooga, Tenn. (Major, MC, AUS)
Clarence H. Boswell, Rockford, Ill. (Lt. Col., MC, AUS)
Russell Stanton Bray, Providence, R. I. (Capt., MC, USNR)
Joseph B. Cady, Sayre, Pa. (Lt. Col. MC, AUS)
Lee D. Cady, St. Louis, Mo. (Col., MC, AUS)
John W. G. Caldwell, Des Moines, Iowa (Squadron Leader, RCAF)
F. Benjamin Carr, Worcester, Mass. (Capt., MC, USNR)
Edward Patterson Childs, New York, N. Y. (Lt. Comdr., MC, USNR)
Abraham G. Cohen, New York, N. Y. (Lt. Col., MC, AUS)
Leon H. Collins, Jr., Philadelphia, Pa. (Lt. Col., MC, AUS)
Charles A. R. Connor, New York, N. Y. (Major, MC, AUS)

Ralph R. Cooper, Detroit, Mich. (Major, MC, AUS)
J. Antrim Crellin, Philadelphia, Pa. (Comdr., MC, USNR)
Constance A. D'Alonzo, Wilmington, Del. (Capt., MC, AUS)
Nicholas John Di Gregorio, Brooklyn, N. Y. (Major, MC, AUS)
Preston V. Dilts, Pittsfield, Ill. (Lt. Comdr., MC, USNR)
Robert Deming Donaldson, Kane, Pa. (Comdr., MC, USNR)
William M. Donovan, Scranton, Pa. (Major, MC, AUS)
Glenn E. Drewyer, Flint, Mich. (Comdr., MC, USNR)
Willard G. Drown, Warren, Ohio (Lt. Col., MC, AUS)
LeRoy B. Duggan, Houston, Tex. (Capt., MC, USNR)
Garfield G. Duncan, Philadelphia, Pa. (Col., MC, AUS)
John Keenan Durkin, Philadelphia, Pa. (Capt., MC, USNR)
John Lewis Dyer, New Orleans, La. (Major, MC, AUS)
Hamblen C. Eaton, Harrisburg, Pa. (Capt., MC, USNR)
Kendall A. Elsom, Philadelphia, Pa. (Lt. Col., MC, AUS)
Harry D. Fein, New York, N. Y. (Capt., MC, AUS)
Arthur N. Ferguson, Fort Wayne, Ind. (Col., MC, AUS)
E. Minton Fetter, San Diego, Calif. (Capt., MC, USNR)
David Finkelstein, Philadelphia, Pa. (Capt., MC, AUS)
Thomas Fitz-Hugh, Jr., Philadelphia, Pa. (Col., MC, USA)
Richard D. Friedlander, San Francisco, Calif. (Lt. Col., MC, AUS)
Mervyn J. Fuendeling, Twin Falls, Idaho (Comdr., MC, USNR)
Delmar R. Gillespie, St. Paul, Minn. (Major, MC, AUS)
Henry Spencer Glidden, Andover, Mass. (Comdr., MC, USNR)
Benjamin E. Goodrich, Pleasant Ridge, Mich. (Capt., MC, USNR)
Henry B. Gotten, Memphis, Tenn. (Comdr., MC, USNR)
Stephen A. Graczyk, Buffalo, N. Y. (Major, MC, AUS)
James R. Gudger, New York, N. Y. (Comdr., MC, USNR)
William R. Hallaran, Cleveland, Ohio (Lt. Col., MC, AUS)
Frank W. Halpin, Fort Worth, Tex. (Lt. Col., MC, AUS)
John Richard Hamilton, Nassawadox, Va. (Comdr., MC, USNR)
Percy Gatling Hamlin, Santa Barbara, Calif. (Lt. Col., MC, AUS)
Joseph E. Harenski, Natrona, Pa. (Major, MC, AUS)
Edward H. Hashinger, Kansas City, Mo. (Col., MC, AUS)
Arthur O. Hecker, Pittsburgh, Pa. (Lt. Col., MC, AUS)
Herman S. Hoffman, Washington, D. C. (Capt., MC, USNR)
Ralph Howard Homan, El Paso, Tex. (Comdr., MC, USNR)
F. Redding Hood, Oklahoma City, Okla. (Lt. Col., MC, AUS)
John Davis Hughes, Memphis, Tenn. (Major, MC, AUS)
J. Warren Hundley, Jr., Philadelphia, Pa. (Lt. Col., MC, AUS)
Arthur Trimble Hurst, Louisville, Ky. (Comdr., MC, USNR)
Samuel Hurwitz, Jamestown, N. Y. (Comdr., MC, USNR)
Milosh Kasich, New York, N. Y. (Lt. Col., MC, AUS)
T. Douglas Kendrick, Utica, N. Y. (Major, MC, AUS)
Richard A. Kern, Philadelphia, Pa. (Commodore, MC, USNR)
Robert W. Kimbro, Cleburne, Tex. (Capt., MC, AUS)
Robert L. King, Seattle, Wash. (Lt. Col., MC, AUS)
Melvin Bryon Kirkstein, St. Louis, Mo. (Capt., MC, AUS)
Leslie R. Kober, Phoenix, Ariz. (Comdr., MC, USNR)
Arthur M. Kraut, Jersey City, N. J. (Lt. Col., MC, AUS)
Harold J. Kullman, Detroit, Mich. (Capt., MC, USNR)
Albert T. Leatherbarrow, Hampton Station, N. B., Canada (Major, MC, RCA)
Aleksei A. Leonidoff, Poughkeepsie, N. Y. (Lt. Col., MC, AUS)

Ralph U. Leser, Indianapolis, Ind. (Major, MC, AUS)
Seaborn J. Lewis, Beaumont, Tex. (Capt., MC, USNR)
McKinley London, Cleveland, Ohio (Comdr., MC, USNR)
Harold C. Lueth, Evanston, Ill. (Lt. Col., MC, AUS)
Mischa J. Lustok, Milwaukee, Wis. (Lt. Col., MC, AUS)
Alexander R. MacLean, Rochester, Minn. (Lt. Comdr., MC, USNR)
Alexander Marble, Boston, Mass. (Col., MC, AUS)
Albert G. Markel, Paterson, N. J. (Comdr., MC, USNR)
Orlando B. Mayer, Columbia, S. C. (Col., MC, AUS)
Johnson McGuire, Cincinnati, Ohio (Col., MC, AUS)
H. Easton McMahon, Plandome, N. Y. (Capt., MC, USNR)
Joseph Medoff, Philadelphia, Pa. (Capt., MC, AUS)
William B. Meister, Newburgh, N. Y. (Col., MC, USA)
William C. Meredith, New Rochelle, N. Y. (Lt. Comdr., MC, USNR)
Louis Merves, Philadelphia, Pa. (Capt., MC, AUS)
Solomon G. Meyers, Detroit, Mich. (Major, MC, AUS)
George W. Millett, San Francisco, Calif. (Comdr., MC, USNR)
John Minor, Washington, D. C. (Col., MC, AUS)
William J. Mitchell, San Marino, Calif. (Lt. Col., MC, AUS)
Flavius D. Mohle, Houston, Tex. (Major, MC, AUS)
Ferrall H. Moore, Redwood City, Calif. (Lt. Comdr., MC, USNR)
Hugh J. Morgan, Nashville, Tenn. (Brig. Gen., MC, AUS)
Carlyle Morris, Metuchen, N. J. (Major, MC, AUS)
John M. Murphy, Detroit, Mich. (Major, MC, AUS)
Clifford K. Murray, Haverford, Pa. (Lt. Comdr., MC, USNR)
Walter L. Nalls, Alexandria, Va. (Lt. Col., MC, AUS)
Louis Ochs, Jr., Shreveport, La. (Lt. Col., MC, AUS)
Hugh B. O'Neil, Plainview, Tex. (Capt., MC, AUS)
Robert Clinton Page, White Plains, N. Y. (Major, MC, AUS)
Oscar A. Palatucci, New York, N. Y. (Lt. Col., MC, AUS)
Felix Roman Park, Bala-Cynwyd, Pa. (Lt. Col., MC, AUS)
Victor L. Pellicano, Niagara Falls, N. Y. (Major, MC, AUS)
D. Sergeant Pepper, Philadelphia, Pa. (Lt. Col., MC, AUS)
Richard O. Pfaff, San Jose, Calif. (Lt., MC, USNR)
Francis D. Pierce, Fort Lauderdale, Fla. (Major, MC, AUS)
Leslie S. Pierce, Greensburg, Pa. (Major, MC, AUS)
J. William Quinlan, Rochester, N. Y. (Lt. Comdr., MC, USNR)
Robert B. Radl, Bismarck, N. D. (Lt. Col., MC, AUS)
Lewis K. Reed, Youngstown, Ohio (Major, MC, AUS)
Henry A. Rothrock, Bethlehem, Pa. (Capt., MC, USNR)
Hendrik M. Rozendaal, Schenectady, N. Y. (Lt. Col., MC, AUS)
Robert B. Rutherford, Peoria, Ill. (Col., MC, AUS)
Israel A. Schiller, Brooklyn, N. Y. (Major, MC, AUS)
S. Stanley Schneierson, New York, N. Y. (Lt. Comdr., MC, USNR)
Carl A. Schuck, Hamilton, Ohio (Col., MC, AUS)
Norman R. Shulack, New York, N. Y. (Major, MC, AUS)
George W. Slagle, Battle Creek, Mich. (Comdr., MC, USNR)
O. Norris Smith, Greensboro, N. C. (Major, MC, AUS)
H. U. Solovay, Brooklyn, N. Y. (Capt., MC, AUS)
Carlton R. Souders, Brookline, Mass. (Capt., MC, AUS)
John Stites, Louisville, Ky. (Major, MC, AUS)
Emile G. Stoloff, New York, N. Y. (Lt. Col., MC, AUS)
William G. Talmage, Succasunna, N. J. (Capt., MC, AUS)

Gurney Taylor, New York, N. Y. (Lt. Col., MC, AUS)
Harry E. Thompson, Tucson, Ariz. (Capt., MC, AUS)
James W. Tice, Hamilton, Ont., Canada (Air Commodore, RCAF)
David S. Traub, Louisville, Ky. (Capt., MC, AUS)
Woodford B. Troutman, Louisville, Ky. (Lt. Col. MC, AUS)
Lorenz M. Waller, Hollywood, Calif. (Col., MC, AUS)
W. Kennedy Waller, Baltimore, Md. (Lt. Col., MC, AUS)
Charles Edward Watts, Seattle, Wash. (Capt., MC, USNR)
Joseph C. Watts, Bayside, Long Island, N. Y. (Major, MC, AUS)
Walter David Westinghouse, Buffalo, N. Y. (Lt. Comdr., MC, USNR)
Winthrop Wetherbee, Jr., Boston, Mass. (Lt. Col., MC, AUS)
T. Preston White, Charlotte, N. C. (Col., MC, AUS)
Carl J. W. Wilen, Manhattan, Kan. (Major, MC, AUS)
Robert J. Williams, Providence, R. I. (Lt. Comdr., MC, USNR)
C. Stuart Wilson, Detroit, Mich. (Major, MC, AUS)
George Campbell Wilson, Norwich, Conn. (Comdr., MC, USNR)
Henry M. Winans, Dallas, Tex. (Lt. Col., MC, AUS)
Walter L. Winkenwerder, Baltimore, Md. (Lt. Col., MC, AUS)
Donald E. Wood, Indianapolis, Ind. (Lt. Col., MC, AUS)
Francis Clark Wood, Phliadelphia, Pa. (Lt. Col., MC, AUS)
Raymond J. Wyrens, Omaha, Nebr. (Capt., MC, AUS)
Lloyd B. Young, Detroit, Mich. (Lt. Comdr., MC, USNR)
William A. Zavod, Mount Vernon, N. Y. (Major, MC, AUS)

Directory

Postgraduate Training Facilities

Internal Medicine and Allied Specialties

The Office of the Educational Director has compiled the following information from replies received from the various University Medical Schools.

University of Chicago
The School of Medicine
1945–1946

Opportunities for post-doctorate work exist in many departments of the Medical School, leading to the degree of S.M. or Ph.D.

The Dean of Students is Dr. Lawrence A. Kimpton, Cobb Lecture Hall, Room 203, University of Chicago, Chicago 37.

Columbia University
College of Physicians and Surgeons
School of Medicine
1945–1946

Columbia-Presbyterian Medical Center
630 West 168th Street
New York 32, N.Y.

Columbia University confers the degree of Doctor of Medical Science on those who complete graduate training over a period of at least three years after the internship in the University or in associated hospitals and laboratories. Only current residents appointed in one of the affiliated hospitals are eligible for registration for the degree.

A wide variety of short courses has been organized in the hospitals and clinics affiliated with the University. These short courses are of two types: Those for the gen-

eral practitioner and those designed to provide advanced instruction, in small groups, to already qualified specialists.

Further information concerning the graduate training (three years) and the short postgraduate courses for practitioners and specialists may be obtained by addressing the Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York 32, N.Y.

Columbia University
New York Post-Graduate Medical School
Department of Medicine

The following courses will be given from March through June, 1946:

360—Combined Course in Internal Medicine. Twelve weeks, March 4 through May 24, 1946. Fee for 12 weeks: $350. Maximum class, thirty. (Enrollment will also be accepted for eleven weeks, March 4 through May 17, fee, $325; and for ten weeks, March 4 through May 10; fee, $300.)

This course is designed to meet the needs of returning medical officers for a refresher course covering the major fields of internal medicine, and preference will be given to discharged medical officers in admission to the combined course. Other physicians will be admitted to the following separate courses: Nos. 342, 330, 343, and 337.

Emphasis is placed on therapy, the importance of adequate nutrition, the psychosomatic aspects, and the rôle of geriatrics in each of the diseases under discussion. Diagnostic and therapeutic procedures are demonstrated. Ample time is allotted for the examination of patients in most of the sections.

The following consecutive courses are included in the combined course:

342—Normal and Pathological Physiology.
Ten days; March 4–15, 1946. Fee, $75.
330—Arthritis and Allied Rheumatic Disorders.
Five days; March 18–22, 1946. Fee, $45.
343—Gastroenterology.
Ten days; March 25–April 5, 1946. Fee, $75.
337—Diabetes Mellitus, Nephritis and Hypertension.
Five days; April 8–12, 1946. Fee, $45.
349—Cardiology.
Four weeks; April 15–May 10, 1946.
Maximum class, thirty. Fee, $125.
1140—Peripheral Vascular Diseases.
Five days; May 13–17, 1946.
Maximum class, twenty-four. Fee, $45.
333—Acute and Chronic Pulmonary Diseases.
Five days; May 20–24, 1946.
Maximum class, fifteen. Fee, $45.

The following additional courses will be given in June, 1946:

345—Electrocardiography.
Five days, June 3–7, 1946. Fee, $50.
348—Parasitology and Tropical Medicine.
Five days, June 3–7, 1946. Fee, $45.
1100—Symposium on Industrial Medicine.
Five days, June 10–14, 1946. Fee, $45.

341—Symposium on Internal Medicine.
Ten days, June 17–28, 1946. Registrations will be accepted for the entire ten days or for either the first or second five-day session. Fees: $45 for five days; $75 for ten days.

Department of Pediatrics

410—Clinical Pediatrics.
Four weeks, April 1–27, 1946. Fee, $125.

Detailed programs of these courses will be sent upon request.

Application should be submitted as far in advance as possible, addressed to The Director of the School, 303 East 20th Street, New York 3, N.Y.

Columbia University
New York Post-Graduate Medical School
Second Avenue at 21st Street
New York 3, N.Y.

Courses in Clinical Medicine, 1945–1946:

1100—Symposium on Industrial Medicine.
Five days; March 18–22, 1946.
Minimum class, ten. Fee, $45.

1140—Peripheral Vascular Diseases.
Five days; May 6–10, 1946.
Minimum class, five; maximum, fifteen. Fee, $45.

1143—Physical Therapy.
Five days; April 22–26, 1946.
Minimum class, ten. Fee, $45.

330—Arthritis and Allied Rheumatic Disorders.
Five days; April 1–5, 1946.
Minimum class, five. Fee, $45.

331—Allergy.
Three weeks; April 1–19, 1946.
Minimum class, four; maximum, eight. Fee, $200.

336—Gastroenterology.
Five days; March 4–8, 1946.
Minimum class, five; maximum, fifteen. Fee, $45.

337—Diabetes Mellitus, Nephritis, and Hypertension.
Five days; May 20–24, 1946.
Minimum class, five. Fee, $45.

339—Cardiology.
Five days; May 13–17, 1946.
Minimum class, five; maximum, thirty. Fee, $45.

341—Symposium on Internal Medicine.
Ten days; June 3–14, 1946. Registrations will be accepted for the entire ten days or for either the first or second five-day session.
Minimum class, ten. Fees: $45 for five days; $75 for ten days.

345—Electrocardiography.
Five days; March 11–15, 1946.
Minimum class, five. Fee, $50.

347—Pathological Physiology: Functional and Chemical Aspects.
Five days; April 8–12, 1946.
Minimum class, five. Fee, $45.

123—Gross and Microscopic Pathology.
2–5 p.m., Monday, Wednesday, and Friday; April 22–May 31, 1946.
Minimum class, three; maximum, eight. Fee, $75.

415—Symposium on Recent Advances in Pediatrics.
Six days, March 25–30, 1946, and June 17–22, 1946.
Minimum class, five. Fee, $50.

Under the direction of Columbia University, postgraduate courses in Clinical Medicine will be given at the Montefiore Hospital, Gun Hill Road (near Jerome Avenue), New York 67; also at the Mount Sinai Hospital, Fifth Avenue and 100th Street, New York 29.

The program at the Montefiore Hospital will be devoted to Cardiology and Electrocardiography, and sessions will be held in the afternoons one or two days a week, from March through August.

The program at the Mount Sinai Hospital will include instruction in Allergy, Venereal Diseases, Gastroenterology, Geriatrics; Cardiovascular Diseases, Neurology and Psychiatry, and the Normal and Pathological Physiology of Water and Electrolyte Balance. These courses will be given on a part time basis, one or two days weekly, from February through the middle of June, 1946.

Graduate courses in Neurology and Psychiatry offered by Columbia University College of Physicians and Surgeons and cooperating institutes will be repeated in October, 1946. These courses are designed for a careful clinical survey of Neurology and Psychiatry, with emphasis on the sociological and educational aspects of these subjects. The entire trimester in Neurology and Psychiatry may be taken for a fee of $250.

Blank form of application for admission may be obtained from Dr. N. D. C. Lewis, Director, Psychiatric Institute, 722 West 168th Street, New York 32, N.Y.

Cornell University Medical College
1300 York Avenue
New York City

The Cornell University Medical College at present does not offer work corresponding to that usually described as clinical postgraduate work. Certain professors in the pre-clinical departments offer graduate instruction as an integral part (Group F) of the Graduate School of Cornell University, leading to advanced degrees. The pamphlet entitled "The Announcement of the Graduate School" should be consulted by the candidate before application for admission.

The Creighton University School of Medicine
Omaha, Nebraska

All departments of the School of Medicine are planning to offer refresher courses for returned veteran medical officers. The Department of Medicine proposes to offer preceptorships in medicine whereby a limited number of students may be assigned to various members in that department. A number of courses of variable length will be given in the following subjects: Cardiovascular Renal Diseases, Gastroenterology, Diabetes, Diseases of the Chest, Endocrinology, General Medicine, Preceptorship, Clinical Pathological Conference, Clinical Basic Science Conference, Bibliography.

Duke University School of Medicine
Durham, N. C.

See item in this directory listed under "Postwar Planning Committee of the Medical Society of the State of North Carolina."

Harvard Medical School
Boston, Mass.

The Harvard Medical School offers a six months course in medicine and surgery providing instruction in the fundamental concepts of medical and surgical practice. This course is available to medical officers upon discharge from the Armed Forces. Use will be made of all of the facilities of the Medical School and its affiliated hospitals. This course is not intended to prepare the student for specialization, but is essentially a review course of basic principles.

The course, beginning February 1, accommodates 35 to 40 men, with provision for subsequent enrollment of 5 or 6 veteran medical officers at monthly intervals up to a total of 60 students.

Application for admission should be made to the Assistant Dean of Courses for Graduates, Harvard Medical School, 25 Shattuck Street, Boston 15, Mass.

Tuition for the course will be $360.00 plus an additional fee of $15.00 for medical care and hospitalization. This plan comes under the provisions of Public Law 346, "G.I. Bill of Rights."

University of Illinois
College of Medicine
Chicago, Illinois

The University of Illinois College of Medicine, Chicago, offers a variety of opportunities for veteran physicians to continue their professional and scientific education, as follows: (1) a 3 months general clinical course; (2) a number of clinical specialty courses for qualified applicants; (3) residencies in clinical specialties in University hospitals and institutes; and (4) graduate courses in basic medical sciences, leading to the degrees of Master of Science and Doctor of Philosophy.

Fees will average approximately $100.00 per quarter, and the entire plan will come under the provisions of the G.I. Bill of Rights.

The above opportunities are available as of February 1, 1946.

Further information may be obtained from the Dean, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

Indiana University School of Medicine
Indianapolis, Indiana

The Indiana University School of Medicine offers four different kinds of postgraduate work for the benefit of returning physicians: (1) a general review of clinical medicine adapted to the needs of the general practitioner; (2) a thorough course of at least 6 months in the basic sciences to prepare candidates for the national board examinations; (3) externe work in the University and City hospitals of 3 to 6 months' duration; and (4) a continuation of the present program of postgraduate training of residents in the various University hospitals and affiliated institutions.

State University of Iowa
College of Medicine
Iowa City, Iowa

The College of Medicine of the State University of Iowa presents two types of opportunities to returning veteran medical officers. The first plan consists of an informal course for which no fee will be charged, and which will provide a review and survey of the present trend in medical teaching and practice by attendance at regular undergraduate classes. The second plan consists of a formal refresher course of at least 3 months' duration, which will be available whenever 10 physicians are accepted, and will be repeated as often as the demand exists. This refresher course will fur-

nish a review of the fundamentals of medical practice, particularly in internal medicine, surgery, obstetrics, gynecology, and pediatrics. Continuation studies in the basic sciences will be provided upon request. The fee for the course is $100. For further information address: The Dean, College of Medicine, Iowa City, Iowa.

University of Kansas
Kansas City, Kansas.

The University of Kansas has organized a Division of Graduate Medical Education for the purpose of providing postgraduate training to veteran and civilian physicians.

The curriculum is designed to meet as nearly as possible the need for additional training for all groups of physicians. Instruction will be available in the basic sciences, in the specialties of medicine and surgery and ancillary subspecialties.

Intensive review courses from 3 to 10 days in length are planned for the benefit of veterans who desire a quick review before returning to practice. Fees will range from $10.00 to $50.00, depending on the length of the course and the nature of the program.

Correspondence should be addressed to the Director, Division of Graduate Medical Education, University of Kansas, School of Medicine, Kansas City, Kansas.

The Long Island College of Medicine
350 Henry Street, Brooklyn, N.Y.

The Long Island College of Medicine, Brooklyn, New York, has published a spring program of postgraduate courses authorized by their Joint Committee on Postgraduate Education. Most of the courses will run from 8 to 12 or 15 sessions, and are limited in registration to 8 or 10 men. Fees vary from $20.00 to $50.00, depending on the length of the course, and presumably can be defrayed through the G.I. Bill of Rights. Special emphasis will be placed on clinical medicine and the allied subspecialties.

Application should be made to the Joint Committee on Post-Graduate Education at the Medical Society Building, 1313 Bedford Avenue, Brooklyn, N.Y.

Mayo Foundation

The Mayo Foundation for Medical Education and Research of the University of Minnesota, Rochester, Minnesota, offers a wide variety of courses in medicine and surgery and hygiene and the various subspecialties.

Detailed information may be obtained from the office of Dr. Donald C. Balfour, Director of the Mayo Foundation.

McGill University Faculty of Medicine
Montreal, Canada

The Faculty of Medicine of McGill University, Montreal, has set forth an extensive program of graduate instruction dedicated to the needs of medical officers returning to civilian life from the Armed Forces of the Dominion. Refresher courses will be given at McGill University and associated hospitals. In addition, courses in graduate study are available with training towards diplomas in internal medicine in the Clinical Departments of the Faculty of Medicine. Diplomas are also offered in surgery, obstetrics and gynecology, pediatrics, psychiatry, neurology, neurosurgery, ophthalmology, otolaryngology, radiology, and urology. In addition to the above, tutorial classes have been established in preparation for the final examinations of the Royal College of Physicians and for fellowship in the Royal College of Surgeons, Canada.

University of Michigan Medical School
Ann Arbor, Michigan

The Medical Faculty of the University of Michigan has announced a postwar program of training and review courses for returning medical officers and civilian physicians. The plan essentially provides a graduate program for resident staff appointees, special instructorships, intensive review courses in general medicine, brief review courses in specialized fields, and clinical exercises for practitioners.

Correspondence concerning postgraduate medical instruction and training at the University of Michigan should be addressed to: Dr. Howard H. Cummings, Chairman, Department of Postgraduate Medicine, University Hospital, Ann Arbor, Michigan.

University of Minnesota Medical School
Minneapolis, Minnesota

The University of Minnesota Center for Continuation Study announces a series of courses for graduates whose plans for continuation education were interrupted by military service.

These courses have been arranged for veteran medical officers who plan to accept an association with a specialist or obtain a residency or prepare for American Board examinations or return to practice. Continuation courses will be offered in medicine, surgery, and the basic sciences. Classes will be taught at the Center for Continuation Study, Medical School, University of Minnesota Hospitals, Minneapolis General Hospital, Ancker Hospital (St. Paul), and affiliated teaching institutions. Communications should be addressed to Dr. William A. O'Brien, Director of Postgraduate Medical Education.

University of Montreal Faculty of Medicine

The Faculty of Medicine of the University of Montreal is prepared to provide to demobilized medical officers refresher courses of 6 to 8 weeks' duration. A maximum of 15 candidates and a minimum of 10 will be accepted. Specialty courses of 2 weeks will follow refresher courses.

New York Polyclinic
Medical School and Hospital
335 to 361 West 50th Street
New York 19, N. Y.

The New York Polyclinic Medical School and Hospital offers practical instruction in all branches of medicine and surgery. A 6 weeks full time course in medicine provides integrated clinical and didactic study, and covers practical problems in diagnosis and treatment. Ample time is devoted to demonstrations in medical specialties, and opportunity is afforded for the matriculant to supplement this course by an additional 6 weeks of work in the wards and out-patient department of the hospital.

A full time course including the fundamentals of the various medical and surgical specialties, and reviewing established procedures and recent advances in medicine and surgery, is also offered for the benefit of the general practitioner.

For further information, address Edward L. Kellogg, M.D., Medical Executive Officer of the New York Polyclinic.

Postwar Planning Committee of the Medical Society of the State of *North Carolina*

The Postwar Planning Committee of the Medical Society of the State of North Carolina has established review and refresher courses at the University of North Carolina School of Medicine (Chapel Hill), at the Bowman Gray School of Medicine of Wake Forest College and the North Carolina Baptist Hospital (Winston-Salem),

and at the Duke University School of Medicine (Durham). An extensive schedule of ward rounds, clinics, and conferences are available to veteran medical officers who may avail themselves of refresher courses of this nature over a period of three months. A limited number of appointments for a minimum period of nine months will provide training leading to certification in the various specialties. A number of fellowships are available for graduate study, and a certain number of residencies are available in medicine and the allied subspecialties.

Northwestern University
Medical School
Chicago, Illinois

The Medical School of Northwestern University has recently organized a program devoted to the satisfaction of the requirements of the American specialty boards for certification. All specialties are included in this program, the fundamental feature of which is the coördination of a group of approximately 150 residencies and fellowships in 10 Chicago hospitals. A Master's degree may be obtained by additional registration in the Graduate School of Northwestern University and the completion of a substantial research project and thesis. Three years is the length of the normal training period; but in the immediate postwar phase, many appointments will be available for shorter periods because of credit for military service allowed by various certifying Boards.

Research assignments are available in all fields of study, but no intensive training of the short review or refresher type is provided. Requests for such training should be referred to the Cook County Graduate School of Medicine, 427 South Honore Street, Chicago—Mr. James Askin, Registrar.

Dr. Arthur R. Colwell is the Director of Medical Specialty Training at Northwestern University, Ward Memorial Building, 303 East Chicago Avenue, Chicago 11.

Ohio State University
Columbus, Ohio

The College of Medicine of Ohio State University has established a program of postgraduate refresher training, designed especially for returning veterans. Opportunities are available in all departments, and will provide for study and observation of ward patients, review of special procedures and technics, clinical dispensary duty, and full access to both preclinical and clinical facilities and resources of the College of Medicine.

Applications for postgraduate refresher training should be made to Dr. George H. Ruggy, Junior Dean, College of Medicine, Ohio State University, Columbus 10, Ohio.

The University Hospital will adopt a program consisting of a 5-year period of training in residence, which will equip physicians to practice a specialty and qualify them for examination by the national certifying board. Advanced degrees are available to those who satisfy the requirements of the Graduate School, Ohio State University.

Applications should be addressed to Mr. Louis Blair, Superintendent, University Hospital, Ohio State University, Columbus 10, Ohio.

University of Oregon Medical School
Portland, Oregon

The Medical School of the University of Oregon offers a refresher course for general practitioners, and intensive courses in cardiology, obstetrics, and pediatrics. In addition, specialty refresher courses are offered in various subjects, and a series

of twelve 5-day intensive courses has been established. The program of approved specialty residencies will be continued and, in addition, a veteran residency program has been authorized for veterans only.

Further information concerning reservations, registration, schedules, class quotas, starting dates, etc., may be obtained from the Director of Postgraduate Training, Office of the Dean, University of Oregon Medical School, 3181 S.W. Marquam Hill Road, Portland 1, Oregon.

University of Pennsylvania School of Medicine and
Graduate School of Medicine
Philadelphia, Pa.

The School of Medicine will offer a refresher course of 12 weeks' duration to those who wish an intensive comprehensive review in medicine, surgery, and the clinical specialties.

Application for enrollment may be made to Dr. Isaac Starr, Dean, University of Pennsylvania School of Medicine, Philadelphia 4, Pa.

The Graduate School of Medicine specializes in Long-term Graduate Training with basic and advanced instruction leading to clinical specialization. At least one academic year of full time study is required. An additional two years of practical experience under an acceptable preceptor and an original thesis will qualify the student for a M.Sc. (Med.) degree. The fee is $800.

In addition, the Graduate School of Medicine presents short courses in clinical specialties for students who are already qualified as specialists. These courses vary in length from 2 weeks to 4 months, and the fees will be commensurate with the length of each course.

Information concerning these excellent opportunities for training may be obtained from Dr. Robin C. Buerki, Dean, Graduate School of Medicine, University of Pennsylvania, Philadelphia 4, Pa.

All of the above plans offered by the University of Pennsylvania come under the provisions of the G. I. Bill of Rights.

University of Pittsburgh
School of Medicine
Pittsburgh, Pa.

The University of Pittsburgh School of Medicine has organized a refresher course of 8 weeks' duration for the general practitioner, constituting a review of all aspects of clinical medicine. Registration will be limited to a group of 20 to 24 veterans. The fee will be $150.00, payable under Public Law 346.

Intensive refresher work in a specific subject will not be offered.

Applications should be addressed to the Dean of the School of Medicine, University of Pittsburgh, Pittsburgh 13, Pa.

University of Rochester
School of Medicine and Dentistry
Rochester, New York

The University of Rochester School of Medicine and Dentistry provides opportunities for postgraduate training of veteran physicians by means of expansion of their residency program in medicine and surgery and special fields. A 6 weeks' refresher course is designed to present a broad reorientation in the whole field of medicine, and will allow for clinical instruction in the special field of a veteran medical officers' particular interest.

A detailed catalog of facilities in Rochester may be obtained from the Assistant Dean, Dr. George Packer Berry, 260 Crittenden Boulevard, Rochester 7, New York.

Southwestern Medical College
Dallas, Texas.

The Southwestern Medical College of the Southwestern Medical Foundation located in Dallas, Texas, offers a 2 months' course in medicine and pediatrics for returning medical officers and other interested physicians. Enrollment will be limited to 20 men, and all communications should be addressed to: Dr. Donald Slaughter, Dean of Students, Southwestern Medical College, 2211 Oak Lawn Avenue, Dallas 4, Texas.

Syracuse University
College of Medicine
Syracuse, New York

The Syracuse University College of Medicine offers opportunities for study, observation, and clinical experience for returning medical officers and civilian physicians. These exercises will include lectures, clinics, bedside rounds, clinical pathological conferences, and laboratory demonstrations.

Intensive instruction in special fields may be offered to a limited number of physicians.

Address all communications to the Dean, College of Medicine, Syracuse University, 766 Irving Avenue, Syracuse 10, New York.

Temple University School of Medicine
Philadelphia, Pa.

Temple University School of Medicine will offer a course in Psychosomatic Medicine for the internist and general practitioner from March 4 to March 30, 1946. The fee for the course is $200. Full details may be obtained by writing to Mrs. Carol Krusen Scholtz, Registrar, 3401 North Broad Street, Philadelphia 40, Pa.

University of Texas
School of Medicine
Galveston, Texas

The School of Medicine of the University of Texas presents an extensive postgraduate program in medicine during the current year. Their general policy is to establish individual arrangements which will satisfy individual needs and preferences for each physician who enrolls in their postgraduate training program, which consists of residency training, preclinical courses, externships, and a series of short courses and conferences in general medicine and surgery and the allied specialties.

Communications should be addressed to the Director, Postgraduate Division, The University of Texas School of Medicine, Galveston.

University of Toronto
Faculty of Medicine

The Faculty of Medicine of the University of Toronto offers a 2 months' refresher course providing instruction in medicine, surgery, obstetrics, gynecology, and pediatrics. This review course for ex-Service medical officers is now under way and will be repeated, beginning April 1, 1946, provided applications are received on or before March 16, 1946.

Tufts Medical School
Postgraduate Division
Boston, Massachusetts

The Postgraduate Division of Tufts Medical School in Boston offers a series of postgraduate courses for the general practitioner. Of interest to internists are the following schedules:

Allergy, May 13–17, 1946
Cardiology, April 29–May 3
Dermatology, April 1–5
Electrocardiography, May 13–17
Endocrinology, May 20–24
Internal Medicine, May 6–31
Proctology, April 22–27 and April 29–May 25
Radiology, April 8–11

Applications for admission should be made to the Chairman, Postgraduate Division, Tufts Medical School, 30 Bennet Street, Boston, Mass.

Tulane University of Louisiana
School of Medicine
New Orleans, Louisiana

The Tulane University of Louisiana School of Medicine, Department of Graduate Medicine, presents a schedule for review of general medical practice, as follows:

Diseases of the Cardiovascular System, March 11–16, 1946
Pulmonary Diseases, March 18–23
Gastrointestinal Diseases, March 25–30
Urinary Diseases, April 8–13
Diseases of Nervous System, April 15–20
Nutritional and Metabolic Diseases, April 22–27
Infectious Diseases, April 29–May 4
Neoplastic Diseases, May 6–11
Obstetrics and Gynecology, May 13–18
Traumatology, May 20–25

Tuition fee is $25.00 per week, and registrants may take as many weeks as desired.

For detailed information write to: Dr. H. W. Kostmayer, Director, Department of Graduate Medicine, 1430 Tulane Avenue, New Orleans 13, La.

Vanderbilt University
School of Medicine
Nashville, Tenn.

The School of Medicine of Vanderbilt University, Nashville, Tennessee, offers postgraduate courses in preventive medicine and public health, and also short intensive courses in clinical subjects. Arrangements have been established between Vanderbilt University and the Commonwealth Fund to sponsor fellowships at Nashville in medicine, surgery, pediatrics, obstetrics, and gynecology.

The Registrar of the Medical School will be glad to supply information upon request.

University of Vermont
College of Medicine
Burlington, Vermont

The University of Vermont offers a 12 weeks' course in general practice for the benefit of returning veteran medical officers. A 4 weeks' review course in internal medicine and another in surgery are available, in addition to 23 elective subjects which may supplement the daily schedule.

Application for enrollment in these courses may be made through the Office of the Dean, College of Medicine, University of Vermont, Burlington, Vt.

Medical College of Virginia
Richmond, Virginia

The Medical College of Virginia plans to offer short courses of the refresher type during the current year. Inquiries should be addressed to: Dr. William B. Porter, Physician-in-Chief, Department of Medicine, Hospital Division, Medical College of Virginia, Richmond, Va.

Washington University
School of Medicine
St. Louis, Missouri

The Washington University School of Medicine, St. Louis, Mo., has authorized an extensive program of postgraduate courses for medical veterans. The Medical School and affiliated hospitals have made provision for postgraduate instruction in the following categories:

1. Residencies and fellowships in all clinical subjects
2. Fellowships in all preclinical sciences
3. A one-month refresher course in ophthalmology
4. A two-month refresher course in otolaryngology
5. An eight-month graduate course in ophthalmology
6. An eight-month graduate course in otolaryngology

Inquiries may be addressed to the Registrar, Washington University School of Medicine, St. Louis 10, Mo.

George Washington University School of Medicine
Washington, D.C.

A program for postgraduate instruction offered by the George Washington University School of Medicine for returning medical officers consists of two essential parts. The first is a series of brief review courses covering a number of the specialties of medical practice, beginning February 11 and extending through April 13, 1946. The following subjects will be stressed: Internal medicine, psychiatry and neurology, pediatrics, infectious diseases, obstetrics, general surgery, gynecology, otorhinolaryngology, ophthalmology, anesthesiology, orthopedics, and urology.

This General Review Course is designed primarily for the man who has previously done general practice, or for the younger veteran who wishes a reorientation in all fields before entering upon further specialty training.

The second part of the program consists of a series of preceptorships in the various specialties for the benefit of medical veterans who have previously had specialty training. These preceptorships under certified specialists vary from a few months to several years' association.

A limited number of fellowships in medicine and pediatrics are available at the University Hospital and other affiliated institutions.

The Dean is Dr. Walter A. Bloedorn, 1335 H Street N.W., Washington 5, D.C.

Wayne University
College of Medicine
Detroit, Michigan

The Wayne University College of Medicine has organized short postgraduate courses, available for veterans only, in the following subjects: Anatomy, pharmacology, physiological chemistry, dermatology, internal medicine, hematology, psychiatry, ophthalmology, and proctology. These courses are an integral part of the Continuation Curriculum at Wayne University College of Medicine.

Further information may be obtained from the Recorder.

University of Wisconsin
Medical School
Madison, Wisconsin

The University of Wisconsin Medical School has established plans for refresher courses and postgraduate training of veteran medical officers. These plans are also available for graduate physicians in civilian practice. The program will consist of four lines of endeavor:

1. A refresher course of 12 weeks' duration for general practitioners.
2. A 2 to 6 months' course for specialists.
3. Residencies of 3 years' duration, leading to specialty certification.
4. Intensive training in the basic sciences for a year or more.

For further information, address: Dean of the Medical School, University of Wisconsin, Madison, Wisconsin.

Woman's Medical College of Pennsylvania
Philadelphia, Pa.

The Woman's Medical College of Pennsylvania offers postgraduate instruction for medical-officers, veterans and civilian physicians. A general clinical refresher course of 3 months' duration will provide quick review of the principal field of internal medicine. The proposed fee for this course is $150.00. Registration will be limited to from 8 to 15 graduate students.

A course in cardiology for advanced students will cover cardiac physiology, clinical cardiology, cardiovascular roentgenology, and electrocardiography. Bedside and out-patient instruction will be provided at the Woman's Hospital and affiliated institutions. Registration will range from 5 to 10 students. The course will be 6 weeks in duration; and the fee, $100.

Further information may be obtained from the Dean of the Woman's Medical College of Pennsylvania, Henry Avenue and Abbottsford Road, Philadelphia 29, Pa.

Canadian veteran medical officers should secure a copy of the booklet entitled "Facts about Your Medical Career on Demobilization," which has been compiled and presented by the Canadian Medical Procurement and Assignment Board, under the authority of the Minister of the Department of Veterans Affairs, and contains general information concerning refresher courses, postgraduate training, placement, and miscellaneous appointments, throughout the Dominion of Canada. This is published by King's Printer, Ottawa, and contains much information of vital interest.

MINUTES OF THE BOARD OF REGENTS

PHILADELPHIA, PA., NOVEMBER 18, 1945

The regular autumn meeting of the Board of Regents was held at the College Headquarters, Philadelphia, November 18, 1945, with President Ernest E. Irons presiding, Mr. E. R. Loveland acting as Secretary, and the following in attendance:

Ernest E. Irons.....*President*
David P. Barr.....*President-Elect*
Walter W. Palmer.....*First Vice President*
James J. Waring.....*Second Vice President*
William D. Stroud.....*Treasurer*
George Morris Piersol.....*Secretary-General*
Jonathan C. Meakins.....
Charles F. Tenney.....
Francis G. Blake.....
Roger I. Lee.....
Charles T. Stone.....
Walter B. Martin.....
William S. Middleton.....
James E. Paullin.....
LeRoy H. Sloan.....
Paul W. Clough.....*Acting Editor,* ANNALS OF INTERNAL MEDICINE
Edward L. Bortz.....*Chairman, Advisory Committee on Postgraduate Courses*
C. C. Shaw.....*Educational Director*

The Executive Secretary read abstracted Minutes of the preceding meeting of the Board, which were approved as read.

The President declared a quorum and requested the Secretary to present communications.

The Secretary read letters from members of the Board who could not be present, chiefly because of transportation difficulties.

PRESIDENT IRONS: Under communications also is a report concerning the discontinuance of the War-Time Graduate Medical Meetings. This was foreshadowed in our meeting last June, and during the interim the American College of Surgeons announced their intention to discontinue this program following the end of the War. I consulted the Executive Committee, and it was its unanimous opinion that the War-Time Graduate Medical Meetings should be concluded, particularly in view of the fact that most Medical Officers now in the Army are thinking more of getting back to their civilian work than they are in advancing their experience in the Service. The American Medical Association, the third participant in this program, likewise, has concurred in its discontinuance. Therefore, it is generally agreed that this program will stop with the current month, or by the first of January, 1946. Again, I think we should express our great appreciation of the efforts of Dr. Edward L. Bortz, and later of Dr. Francis F. Borzell, who, along with representatives of the College of Surgeons and the American Medical Association, have done such a magnificent job. The Chair will entertain a motion to approve the action of the Executive Committee in terminating War-Time Graduate Medical Meetings, and expressing to the members of the sub-committee, as well as to our representatives, our appreciation of their efforts.

. . . On motion by Dr. Jonathan C. Meakins, regularly seconded, a resolution as proposed was unanimously adopted. . . .

PRESIDENT IRONS: Another communication came from the National Academy of Sciences, requesting that the College take a position with respect to the maintenance

of standards by the U. S. Civil Service Commission in the filling of positions of various types, having to do with scientific work. It seemed to your Chairman that the College could speak only for those questions concerning medicine. We were asked to be a little broader in our statement, but it seemed wiser to confine our remarks to those subjects closely allied with medicine, and so a letter was formulated to the National Academy, to the Chairman of the National Research Council, stating that the College feels that standards already established in medicine should be maintained, and for technicians in fields ancillary to medicine standards had already been set up by the Council on Medical Education and Hospitals of the American Medical Association and these should be maintained, and, further, that the College feels that it is not in a position to comment on standards in other professions. The reply was approved by the Executive Committee and dispatched.

MR. LOVELAND: I have a communication and check from Dr. Willard O. Thompson, Chicago, depositing in the Postgraduate Fund of the College a balance of $713.30 from a course conducted for the College a year ago by Dr. Thompson, representing an unused balance, suggesting it be accepted for use in connection with any postgraduate activities of the College in the Chicago area.

. . . On motion by Dr. Roger I. Lee, regularly seconded and unanimously carried, this contribution was acknowledged with deep appreciation. . . .

MR. LOVELAND: Also in the form of a communication, I have to record that Dr. Louis E. Viko, College Governor for Utah, at the request of President Irons, was the official representative of this College on the occasion of the inauguration of the new President of Utah State Agricultural College.

PRESIDENT IRONS: We will now ask for the report of the Executive Secretary.

MR. LOVELAND: Your Executive Secretary thinks it appropriate to make a brief summary report on his activities through the past year. You will learn more of the details, which will be embodied in Committee reports later.

Membership: There has been some gradual falling off in the number of candidates for Associateship and Fellowship during the War, yet that does not necessarily mean there is less membership activity; because of the large number of Associates on military duty who could not present their credentials for Fellowship, there has been a material increase in the amount of correspondence necessary, and we have at all times extended such advice and assistance to these members as has been possible. There is a noticeable increase in the number of inquiries received concerning membership, and we predict from this point forward there will be a marked increase in the number of candidates. The College influence during the War has spread beyond the confines of our own country. Fellows of the College in the Armed Forces have carried the reputation and name of the College to many lands. Witness a letter we received from a physician in Australia, who is a Fellow of the Royal College of Physicians and a Fellow of the Royal Australasian College of Physicians, who said that he had been greatly impressed by his contacts with several of our Fellows in his country, especially because of their great loyalty to the College and their reports on the sterling worth of our organization. He asked that he might too be considered for membership in our College, because he would esteem it not only an honor, but a great privilege to be associated with this organization. We have also received several letters from our members who have shown genuine appreciation of what the College has done during the War, and of our continuing interest in them.

I would remind you that we have a tedious and rather big task in establishing individual records for every Associate who is on military service, in order that we may determine exactly the additional time he has available to qualify for Fellowship. A part of this effort must also be directed toward getting each Associate back into active status and determining the date when he resumes payment of dues.

Membership Roster and Directory: In the early part of the summer we launched upon the project of preparing a new Membership Roster. A considerable amount of

work had already been concluded before D-Day, but with the coming of VJ-Day, the impracticability of completing the Roster was wholly apparent. Our more than 1,900 members in Service were shifted in all directions, some started being separated from the Service, our address lists were greatly affected and the work we had already concluded would have had to be revised. It appeared more practical to us to abandon the whole project for the current year and wait until 1946. We shall want advice from the Regents as to whether they would wish us to undertake the publication of a complete Directory in 1946—a Directory that shall include all the customary information published about each member before the War in our regular editions. To our knowledge, 1,927 of our members served in the Armed Forces; already about 225, or about 12%, have been retired. We have no information on which to base our estimates of how many members will still be in the Service by July 1, 1946, but it is to be presumed that the majority of the Reserve Medical Officers may then be retired.

Annals of Internal Medicine: Following the onset of the War and the waiver of fees and dues to members, we were faced with a considerable diminution in income. At that time we expressed to you our intention to concentrate on increasing the income which we might obtain from other sources, especially from our journal. We are gratified that we were able to increase the circulation of the journal by more than 42%, and the income from advertising 52%.

Postgraduate Courses: In spite of the fact that the Chairman of the Committee on Postgraduate Courses has not been available, due to service in the Pacific, we have nevertheless extended the number of our courses and greatly increased the number of registrations. This feature of the College activity has become so popular, especially with the returning veterans, that for the period these courses are being conducted, a tremendous amount of time is required on the part of the College Staff.

Regional Meetings: Our Regional Meeting program, as you know, has been greatly extended until the current year, when the meetings had to be curtailed due to War restrictions. Nevertheless, a later report from one of the Committees will show that we have been active, nevertheless, and are again resuming several of these meetings. It is our prediction that many of the Governors, and a whole host of our Fellows and Associates will wish to have these Regional Meetings continued on the multi-State basis, even after the resumption of our Annual Sessions. These meetings have been inspiring, filled with good fellowship, and have kept the contacts of the College with its members alive and flourishing.

Educational Director: By direction of the Board of Regents, at its June meeting, the President, the Secretary-General, and the Executive Secretary were instructed to locate and appoint an Educational Director. Several candidates were interviewed and several more were contacted by mail. The Secretary-General, Dr. Piersol, and I interviewed, among others, Dr. C. C. Shaw, and after telephone consultation with President Irons, his appointment was made on November 1, 1945. During the interim, we have succeeded in obtaining for him a competent secretary, and he is busily engaged in organizing his work. From the beginning, he will take over as his responsibility, under such assistance and advice as we can offer, the planning of the Postgraduate Course program, the post-war returning veterans program and the handling of applications for Research and Clinical Fellowships.

College Headquarters: The physical aspects of the College Headquarters building and grounds have been maintained in good condition, but the time will soon come when some replacements will be necessary, both in office equipment and furnishings—in the latter case, especially some of the rugs. The adjoining property, to the south of the Headquarters, also has been maintained in good condition, and is profitably rented. We have not given up the hope that some time in the future we may interest some other medical groups in the adjoining property as their headquarters.

Office Personnel: Our greatest difficulty and burden during the past year has actually been that of obtaining and retaining competent office personnel. Several em-

ployees have been replaced several times during the War. More lucrative positions have been available in War industry and we have not escaped from the labor unrest current throughout the country. The work of the College must go on, and in the emergencies that have arisen through stenographers and secretaries leaving, we have had to compete with industry in obtaining competent replacements. The result is that it is now costing the College much more for office salaries than before the War. With the expanding activities of the College and the absolute necessity to do our work promptly and well, it must be anticipated that the cost of office service will be higher than heretofore. As yet in this area, there is little evidence of any change occasioned by the termination of War contracts, etc. In fact, in most of the cities over the country, the situation appears to be growing more stringent, not only in available labor, but in housing conditions. Many of our returning members cannot locate office space in which to resume the practice of medicine.

Our best services are pledged to the College!

President Irons: I would like to make reference to the accomplishments of one of the members of our Board. This is without intent to fail to recognize the tremendous services of other members. Dr. William S. Middleton has done an exceedingly good job in England, and the standing of the College there has been greatly enhanced thereby. I cannot help from remarking on the tremendous help that he was not only to the College, but in maintaining the interests of the Medical Officers, particularly in reference to their certification in the American Board of Internal Medicine. We will now have the report of the Secretary-General, Dr. George Morris Piersol.

The Secretary-General, Dr. Piersol, reported the deaths of 25 Fellows and 4 Associates since the last meeting of the Board, as follows:

Fellows

Baumgarten, Walter	St. Louis, Mo.	August 23, 1945
Brady, Jules M.	St. Louis, Mo.	September 6, 1945
Breisacher, Leo	Detroit, Mich.	April 29, 1945
Breuer, Miles John	Los Angeles, Calif.	October 14, 1945
Burnett, Thomas Ward	M.C., U. S. Army	October 19, 1945
Comroe, Bernard Isaac	Philadelphia, Pa.	September 14, 1945
Ferguson, Donald Renwick	Philadelphia, Pa.	August 27, 1945
Frost, Kendal	Los Angeles, Calif.	September 28, 1945
Groat, William A.	Syracuse, N. Y.	September 9, 1945
Harrop, George A.	Princeton, N. J.	August 4, 1945
Harvey, John Goold	Detroit, Mich.	May 24, 1945
Hecker, Friedrich A.	Ottumwa, Iowa	June 3, 1945
Jones, Clement R.	Pittsburgh, Pa.	September 3, 1945
McFarland, Joseph	Philadelphia, Pa.	September 22, 1945
Miner, Frederick B.	Flint, Mich.	April 26, 1945
Richardson, W. W.	Mercer, Pa.	June 10, 1945
Sawyer, John P.	Cleveland Heights, Ohio	June 17, 1945
Shepard, Benjamin A.	Kalamazoo, Mich.	June 16, 1945
Smith, William H.	Goldsboro, N. C.	September 29, 1945
Stewart, Alexander Hamilton	Harrisburg, Pa.	July 31, 1945
Streker, William S.	Providence, R. I.	July 8, 1945
Tucker, Beverley R.	Richmond, Va.	June 19, 1945
Watson, William V.	Toronto, Ont., Canada	October 20, 1945
Welch, Paul Brown	Coral Gables, Fla.	May 6, 1945
White, Arthur W.	Oklahoma City, Okla.	June 11, 1945

Associates

Downs, Charles McCabe	M.C., U. S. Army	June 1, 1945
Inman, Jesse Headen	Bakersfield, Calif.	July 15, 1945
Luft, Raymond	Norwood, R. I.	June 23, 1945
Shoup, Jesse	Washington, D. C.	July 21, 1945

. . . At the suggestion of President Irons, the Board stood in memory of those deceased, and particularly in respect to Dr. Clement R. Jones, who for many years was Treasurer of the College. . . .

Dr. Piersol then reported the following list of 13 additional Life Members since the last meeting of the Board, making a grand total of 400, of whom 34 are now deceased, leaving a balance of 366 (named in the order of subscription):

Sydney E. Johnson	Louisville, Ky.
Fred M. F. Meixner	Peoria, Ill.
Hugo O. Altnow	Minneapolis, Minn.
Harold C. Ochsner	Indianapolis, Ind.
Harry Plummer Ross	Richmond, Ind.
Merton M. Minter	San Antonio, Tex.
Samuel L. Crow	Asheville, N. C.
James F. Anderson	Los Angeles, Calif.
Alexander S. Wiener	Brooklyn, N. Y.
Theodore L. Squier	Milwaukee, Wis.
Frank W. Otto	Los Angeles, Calif.
J. M. Nielsen	Los Angeles, Calif.
Ernest D. Hitchcock	Great Falls, Mont.

. . . On motion by Dr. James E. Paullin, regularly seconded and carried, the report of the Secretary-General was adopted. . . .

PRESIDENT IRONS: Under new business and reports, we shall first have a report from the Committee on Credentials, Dr. George Morris Piersol, Chairman.

DR. PIERSOL: The Committee on Credentials held its regular meeting yesterday. There were 120 candidates for Fellowship under consideration, disposed of as follows:

Recommended for Advancement to Fellowship	72
Recommended for Election to Direct Fellowship	9
Recommended for Election First to Associateship	5
Deferred	22
Rejected	12
	120

. . . On motion by Dr. Piersol, on behalf of the Credentials Committee, regularly seconded and unanimously adopted, the following 81 candidates were elected to Fellowship: (*List published in December, 1945, issue*).

DR. PIERSOL (continuing): 145 candidates were considered for Associateship, and disposed of as follows:

Recommended for Election to Associateship	94
Deferred	31
Rejected	20
	145

In addition to the above, 5 candidates for direct Fellowship were likewise recommended for election first to Associateship, making a total of 99 on the recommended list.

. . . On motion by Dr. Piersol, on behalf of the Credentials Committee, regularly seconded and unanimously adopted, the following 99 candidates were elected to Associateship: (*List published in December, 1945, issue*).

Dr. Piersol (Continuing): The following is a report on the candidates elected to Associateship five years ago, December 15, 1940:

Advanced to Fellowship	76
Resigned	1
Time Extended because of Military Service	39
Dropped for Failure to Qualify	28
	144

Those who have failed to qualify for advancement to Fellowship, must now be dropped, in accordance with provisions of the By-Laws.

At the last meeting of the Board of Regents the Committee on Credentials recommended the clarification of qualifications for membership in the College and the raising of standards. A motion was proposed requiring that certification by the American Board of Internal Medicine be a prerequisite for Associateship. This aroused much discussion. The matter was not acted upon, but very wisely deferred until this meeting of the Board. The proposal has been more thoroughly explored during the interval, and Dr. Chauncey W. Dowden, Chairman of the Board of Governors, has conferred with that Board, and has analyzed and briefed their replies, and the abstract thereof is available here for any who may be interested. It constitutes a large document, and I shall not take time to read it. It is apparent, with very few exceptions, that the Board of Governors is opposed to this change in the requirements. The Committee on Credentials, individually and collectively, took occasion to discuss this matter with various members of the College and of the Board of Regents. It is now apparent that the proposed change has disadvantages which would seem to offset its advantages. In the first place, it would considerably increase the age at which men would be able to enter the College; in the second place, it would eliminate the five-year period, which is now a definite inspirational term, and these young men would have removed from them the stimulus that heretofore has existed. Furthermore, the Credentials Committee would experience greater difficulties in setting up certain standards for Fellowship. Still further, if no limitation were to be placed on the term of Associateship, because the new proposal provided that an Associate could remain in that status as long as he chose, a situation would be created in which the dominant group in the College would be Associates; the minority would be Fellows; therefrom, a considerable amount of controversy and even factional strife might possibly arise. More important, perhaps, than any of the other considerations, is the fact that had the proposal been adopted, the College might readily be saddled with a large group of Associates for life. No matter how careful the Committee on Credentials might be, there would be no assurance that some of the young men elected to Associateship might in time be found to be undesirable members later on, and there would be no remedy, whereas at the present time an Associate must qualify for Fellowship within a maximum term of five years, or be discontinued on the Roster.

The Credentials Committee, after considering these objections, is not now inclined to press the matter of adoption of the previous recommendations. It does, however, feel convinced that the present regulations and rules that have been drawn up are totally inadequate. We must set up other more clear-cut and satisfactory criteria

upon which to base the election of Associates. The Committee is confronted with its most difficult task in the election of Associates. It is much better not to elect a man as an Associate than, having taken him in, to terminate his membership.

The Committee, therefore, proposes a motion that the Chair appoint a Committee of five, composed of two members from the Board of Regents, preferably not members of the Committee on Credentials, two members of the Credentials Committee and one from the Board of Governors, to explore the whole situation with regard to admission requirements, and to bring in at the next meeting of this Board definite, carefully considered recommendations.

. . . The motion was seconded by Dr. James E. Paullin, and, after general discussion, was unanimously adopted. . . .

President Irons appointed the following Committee:

From the Board of Regents:	Dr. William S. Middleton, Chairman
	Dr. James E. Paullin
From the Credentials Committee:	Dr. George Morris Piersol
	Dr. Wallace M. Yater
From the Board of Governors:	Dr. George H. Lathrope

. . . On motion by Dr. James E. Paullin, seconded and regularly carried, the report of the Committee on Credentials was adopted as a whole. . . .

PRESIDENT IRONS: Next is the report of the Committee on Public Relations, Dr. Roger I. Lee, Chairman.

DR. LEE: The meeting of the Committee on Public Relations was held November 17, with Dr. Ernest E. Irons and Dr. Lee present, and with the benefit of Dr. James J. Waring and Dr. Francis G. Blake sitting in. The Committee had a communication from the National Advisory Health Council and the National Advisory Council, regarding the National Research Foundation, which is the so-called Bush Report with the corresponding legislation. This was a report broadcast to all medical bodies. The Committee discussed in full various aspects of the present legislation, proposed legislation in regard to the so-called National Research Foundation. The Committee recognized at once that the old situation is in a state of flux and change. The Committee also recognized that the American College of Physicians, together with the American College of Surgeons and the American Medical Association, participates in a joint Committee on Post-War Medical Service, and that this Committee has a sub-committee on the very subject and has made an extensive report under the Chairmanship of Dr. Francis G. Blake.

The Committee endorses the general principles of the so-called Bush Report with particular reference to freedom of research. The Committee endorses the report of the sub-committee of the Joint Committee on Post-War Medical Service, and requests that this report be circularized to the Board of Regents and the Board of Governors; furthermore, that this report, with the endorsement of the Regents of the American College of Physicians, be sent to Senators Kilgore, Magnuson, and other individuals, also to the Joint Committee on Post-War Medical Service, and published in the "Annals." This matter is of very great importance to all members of the medical profession and of the College, and various changes from time to time will be suggested in these Bills. A general report of endorsement seems to the Committee to be much preferable to anything that is more specific. The Committee has a very acute appreciation of the fact that a good many physicians, a good many members of the College, Regents and Governors, have no real first-hand knowledge of this important subject, and it feels by circularizing in this fashion and publication of this report in the "Annals" that information may be spread. I move the adoption of this portion of the report.

. . . The motion was seconded and opened for discussion. . . .

DR. WALTER W. PALMER: I am delighted with the recommendations of the Committee on Public Relations. A large number of the two Committees, one of which is headed by me, met in Baltimore last Wednesday, with the view of organizing for political purposes; that is, to get some money to work. There are two Bills really important, the Kilgore and the Magnuson Bills. Medicine is concerned with what Kilgore may be standing out for, a political appointment of a director, and an Advisory Committee which will have on it representatives from the Services. We feel liaison relationship between a committee of that sort is far preferable. The Kilgore group is changing its Bill almost daily; it is difficult to know where they stand; so our two Committees last Wednesday agreed to stick to principles and not compromise, to organize a committee with a chairman, Homer Smith, and we may want to get your help in writing to Senators and Representatives later on.

DR. FRANCIS G. BLAKE: I am very pleased with the action of the Committee. However, action of this kind without compromise backs the Bush Report point of view, with particular reference to the necessity for freedom of research, if a National Research Foundation is to be established, and should be of value; at least in changing the points of view in Congress, where a National Research Foundation is looked upon merely as a means of coördinating research by federal bureaus. That does not meet the problem at all.

DR. JAMES J. WARING: I too am most gratified that this action has been recommended by the Committee on Public Relations. All the members of the College ought to be deeply concerned and ought to be thoroughly informed about this matter, and ought to make their opinions known in Washington, not only by a resolution of this nature, but by letters addressed to their Representatives.

. . . The motion was unanimously adopted. . . .

DR. LEE (Continuing): The Committee reviewed the cases of one Fellow and one Associate who are disabled and out of practice, and provided for the waiver of their dues for 1945 and until their recovery and resumption of work in the future. The Committee also reviewed the resignation of one Fellow and recommended that inasmuch as his resignation was caused by a disabling illness, that he be retained on the Roster and his dues waived for 1945 and until his recovery and resumption of practice.

. . . On motion by Dr. Lee, seconded and regularly carried, the recommendations concerning the fees and dues cases and the case of resignation were approved and the Committee's report was accepted as a whole. . . .

PRESIDENT IRONS: Next will be the report of the Committee on the Annals of Internal Medicine, Dr. Walter W. Palmer, Chairman.

DR. PALMER: The Chairman met with Dr. Clough and Dr. Irons at the College Headquarters on November 17, at 4:00 p.m. Drs. Fitz and Waring could not be present. The Executive Secretary had prepared a cost analysis, which is submitted:

Comparative analysis for the past six Volumes, ending June 30, 1945

With regard to volume, circulation and costs, it is to be noted that there has been a slight decrease, because of the War, in the amount of scientific matter, an increase in the amount of news notes, a very marked increase in the amount of paid advertising, and a marked increase in circulation. As a matter of fact, the circulation at the present time exceeds 7,500 copies per month, but it is anticipated that due to Army cancellations, there will be a decrease of perhaps a thousand copies per month in the course of the next year. Particularly should be noted the marked increase in the surplus from operations. This surplus has been extremely valuable in carrying on the work of the College during the period when our other income was greatly reduced, because of the absence of annual exhibits and the waiver of dues

of members on military duty. It is not reasonable to expect the surplus to be as great for the coming year as in the past year, because it is certain that many of the military orders will be eventually cancelled. As a matter of fact, cancellations are starting now to come in.

The desirability of seeking more book reviews was discussed. It was suggested that the Editor make a list of suitable reviewers in the several fields of medicine, solicit coöperation and refer worth while books for reviews from them to him.

During the past year the Committee has approved the expenditure of $800.00 to cover the cost of colored plates in publishing an excellent article on hepatitis by Dr. C. J. Watson, of Minneapolis.

The group considered the request of Hubert Winston Smith to publish in the ANNALS a series of articles on medico-legal topics. Such a series, under his supervision, was published three years ago. It was decided to refer the matter for an expression of opinion from the Board of Regents before making final recommendations to the Editor.

Again the Committee wishes to express its appreciation to the Editor and to the Executive Secretary for the success of the ANNALS OF INTERNAL MEDICINE.

The Committee would particularly like to have the Regents express their opinion for or against another issue of the ANNALS devoted to medico-legal medicine under Dr. Smith's supervision.

. . . There was general discussion, for the benefit of the Editor's direction, among various members of the Board, including Doctors Piersol, Lee, Palmer and Mr. Loveland, and the general reaction to publish another issue on this subject was unfavorable. . . .

. . . On motion by Dr. David P. Barr, seconded by Dr. James E. Paullin, the report was adopted. . . .

PRESIDENT IRONS: Next is the Acting Editor's report, Dr. Paul W. Clough.

DR. CLOUGH: The ANNALS has been published about as usual. There is just as much difficulty in the printing establishment in getting the journal out promptly. So far as material is concerned, it is coming in a little better and the quality of material is also better. We have enough material on hand to carry through March or April, as far as main articles are concerned. We will still welcome any good articles from members of the Board of Regents, or from others. It is possible now to resume the use of better paper and to make our journal more presentable. Dr. Pincoffs, the Editor, is recuperating from a major operation at the Walter Reed General Hospital, and although he is now at home, he is not well enough to take up any business topics. However, as far as I am aware, he expects to resume his work as Editor in the not very remote future. For that reason I have not taken any adequate measures to carry out the suggestions that were made at the last Regents' meeting in regard to establishing comprehensive reviews, but shall leave it to Dr. Pincoffs to make plans as he sees fit. We have, however, accepted a few short review articles covering the field of allergy in general, and allergy in reference to rheumatic fever in particular. Unless I receive more enthusiastic support from the Regents with regard to the publication of the medico-legal material by Hubert Smith, I shall not take the matter up further.

. . . On motion by Dr. Palmer, seconded and regularly carried, the report of the Acting Editor was adopted. . . .

PRESIDENT IRONS: Next will be the report of the Committee on Fellowships and Awards, Dr. Francis G. Blake, Chairman.

DR. BLAKE: A meeting of this Committee was held at 2:00 p.m., November 17, with Dr. Jonathan C. Meakins, Dr. C. C. Shaw, as Educational Director, and Dr. Blake present. The Committee reviewed numerous applications for Research Fellowships and Clinical Fellowships, and reports as follows:

Candidates for Research Fellowships: The Committee approved the applications of the following candidate:

Kenneth Austin Evelyn, Montreal, Que., Canada—to work in the Department of Pathology, McGill University, under Professor Duff, and at the Royal Victoria Hospital under Dr. Jonathan C. Meakins on the Pathogenesis and Treatment of Hypertension. Stipend recommended, $2,500.00.

Candidates for Clinical Fellowships: The Committee approved the applications of the following candidates:

Joseph Michael Barker, Arlington, Va.—to work with Dr. Frank Wilson, University of Michigan Hospital. Stipend recommended, $3,000.00.

Norman Leo Cressy, Beverly, Mass.—to work in the Department of Medicine at Yale University under Dr. Francis G. Blake. Stipend recommended, $3,000.00.

John Bamber Hickam, Dayton, Ohio—to work with Dr. Stead at Emory University. Stipend recommended, $2,500.00.

John Scott Hunt, Lexington, Ky.—to work with Dr. Hugh J. Morgan at Vanderbilt University. Stipend recommended, $2,000.00.

Philip Anthony Tumulty, Washington, D. C.—to work at the Johns Hopkins Hospital under Dr. Warfield Longcope. Stipend recommended, $2,500.00.

. . . On motion by Dr. Blake, seconded and unanimously carried, the awarding of the above fellowships was approved and confirmed. Also on motion by Dr. Blake, seconded and unanimously adopted, it was RESOLVED, that four other applications for Research Fellowships and three other applications for Clinical Fellowships be declined. . . .

DR. BLAKE (Continuing): *The John Phillips Memorial Award, 1946*—No action has been taken by the Committee to date with respect to the John Phillips Memorial Award, but the usual list of individuals in the College will be circularized now in respect to recommendations for this Award, and as soon as replies have been received the Committee will report with respect to its recommendations. These will have to be submitted to the Executive Committee for action. Incidentally, the complete files on all the candidates for fellowships are available at the College Office, if any member of the Board wishes to examine them more in detail.

DR. PALMER: Does the recipient of the Phillips' Award have to be an M.D.?

DR. BLAKE: No. I think there have already been Awards to scientists who were not M.D.'s.

DR. BARR: May I ask the distinction between Research and Clinical Fellowships, as offered by the College?

DR. BLAKE: That is a pertinent question. All of these five men, to whom fellowships have been awarded, with the possible exception of one, in addition to wanting additional training in medicine, are types of individuals who will engage also in clinical investigation. To try to draw a sharp distinction between the five Clinical Fellows and the one Research Fellow, except for their particular field of interest, is perhaps difficult, except that it is the plan of all to engage in clinical work, as well as such research work as they may wish to do.

. . . In subsequent discussion, it was brought out that possibly the Clinical Fellowships are more of the character of residencies, whereas the Research Fellowships are clearly for research work. . . .

. . . On motion by Dr. Blake, seconded and carried, the report of the Committee on Fellowships and Awards was adopted as a whole. . . .

PRESIDENT IRONS: Next will be the report of the Committee on Educational Policy, Dr. Roger I. Lee, Chairman.

DR. LEE: This Committee met November 17, and those present included Dr. Irons, ex-officio, Dr. Waring of the Advisory Committee on Postgraduate Courses, and myself, with Dr. C. C. Shaw, the Educational Director. The Committee reviewed the program of Postgraduate Courses offered during the autumn of 1945, for which the registration was as follows:

Course	Associates	Fellows	Non-Members	Total	Army	Navy	U.S.P.H.S.	Civilians
No. 1	19	42	8	69	11	6	2	50
No. 2	15	30	14	59	23	0	2	34
No. 3	9	11	14	34	9	5	2	18
No. 4	26	64	0	90	9	0	3	78
No. 5	27	62	127	216	100	8	2	106
No. 6	25	40	43	108	51	3	3	51
No. 7	32	75	1	108	14	4	1	89
	153	324	207	684	217	26	15	426

The Committee, under new business, reviewed the proposed schedule of Postgraduate Courses for 1946. These courses were selected in view of the experience with past courses in popularity. It is desired not to overwork certain individuals in certain places. The proposed schedule is wholly tentative, but the Committee approves in general the courses outlined below and recommends to the Board of Regents that the Educational Director proceed, with the understanding that there will be, of necessity, changes and adjustments.

Spring, 1946:

1. ALLERGY—Massachusetts General Hospital, Boston—Dr. Francis M. Rackemann, Director.
2. CARDIOLOGY—University of Virginia Department of Medicine, Charlottesville—Dr. J. Edwin Wood, Jr., Director.
3. CARDIOLOGY—Woman's Medical College of Pennsylvania, Philadelphia—Dr. William G. Leaman, Jr., Director.
4. CHEMOTHERAPEUTICS—Washington University School of Medicine, St. Louis—Dr. W. Barry Wood, Jr., Director.
5. GASTRO-ENTEROLOGY—Graduate Hospital, University of Pennsylvania, Philadelphia—Dr. Henry L. Bockus, Director.
6. GASTRO-ENTEROLOGY—Mayo Foundation, Rochester—Dr. Walter C. Alvarez and Dr. E. H. Rynearson, Directors.
7. GASTRO-INTESTINAL DISEASES—Massachusetts General Hospital, Boston—Dr. Chester M. Jones, Director, possibly in conjunction with a course in Pathology of Internal Diseases under Dr. Tracy Mallory, Director.
8. GENERAL MEDICINE—Emory University School of Medicine, Atlanta, Ga.—Dr. James E. Paullin, Director.
9. HEMATOLOGY—Ohio State University College of Medicine, Columbus—Dr. Charles A. Doan, Director.
10. INTERNAL MEDICINE—Harvard Medical School, Boston—Dr. James H. Means, Director.
11. INTERNAL MEDICINE—University of Minnesota Center for Continuation Study, Minneapolis—Dr. W. A. O'Brien and Dr. Cecil J. Watson, Directors.
12. INTERNAL MEDICINE—University of Texas Department of Medicine, Galveston—Dr. Charles T. Stone, Director.

13. INTERNAL MEDICINE—Stanford University Medical School, San Francisco—Dr. Stacy R. Mettier, Director.
14. PHYSIOLOGY OF DISEASES—Harvard Medical School, Boston—Dr. George Thorn, Director.
15. PSYCHIATRY AND NEUROLOGY—Institute of the Pennsylvania Hospital, Philadelphia—Dr. Edward A. Strecker, Director.
16. NEUROLOGY (an alternate for course above)—Northwestern University Medical School, et al, Chicago—Dr. Roland Parks Mackay, Director.

Autumn, 1946:

1. GENERAL MEDICINE—Johns Hopkins University School of Medicine and University of Maryland School of Medicine, Baltimore—with one director from each institution.
2. INTERNAL MEDICINE—McGill University Faculty of Medicine, Montreal—Dr. Jonathan C. Meakins, Director.
3. METABOLIC DISEASES AND NUTRITION—University of Cincinnati College of Medicine, Cincinnati—Dr. M. A. Blankenhorn and Dr. Tom D. Spies, Directors.
4. PERIPHERAL VASCULAR DISEASES—University of Pennsylvania School of Medicine, Philadelphia—Dr. Isaac Starr, Director.
5. PERIPHERAL VASCULAR DISEASES—Mayo Foundation, Rochester—Dr. E. V. Allen, Director.
6. PSYCHIATRY AND NEUROLOGY—University of Wisconsin Medical School, Madison—Dr. Hans H. Reese, Director.

Also submitted for consideration, some time in the distant future, was a course in General Medicine at the University of Mexico, at Mexico City, under Dr. Francisco de P. Miranda, Director.

The Committee discussed at some length an attempt to correlate these courses, because it appears there are various Fellows of the College, some of them distinguished Fellows, who like to see what is going on in other places and in various departments, some of them taking off two or three months to take courses in New York, Philadelphia, Baltimore, Chicago and the West. Experience thus far indicates that all these courses will prove desirable, and many of them will be oversubscribed. As the Executive Secretary has already said today, we should get the registration of these courses down "from a convention to a class."

. . . On motion by Dr. Lee, seconded and regularly carried, the schedule of proposed courses was approved; likewise, the report as a whole was approved. . . .

MR. LOVELAND: I wish to obtain the advice of the Regents with regard to the registration fees for these courses—from members, from non-members and from those in the Armed Forces. Throughout the War no charge whatsoever has been made to a man on active duty in the Armed Forces. This applied both to members and non-members. However, we took non-members only when accommodations were adequate to admit them. How much longer shall the registration fee be waived for members of the Armed Forces? Members? Non-members? We have observed that those to whom we give waiver of the registration fee have not been as careful to notify us when they are unable to attend a course. Perhaps they have not attached great importance to this, even though we have emphasized the necessity of sending in cancellations in advance, so that other physicians could be accommodated. This may be due to the fact that things that come free usually are not evaluated as worth very much. From a practical standpoint, not financial, I have wondered if there should not be at least some small charge, possibly a half of the usual fee, to the men on military service in the future.

PRESIDENT IRONS: May we have discussion by the Regents?

DR. WALTER B. MARTIN: I believe there should be a fee. I think it is bad to admit these men entirely without fee to courses of this kind. A nominal fee would be appropriate.

DR. LEROY H. SLOAN: I do not think the fees charged at present are high enough for what the men are getting. I am in favor of raising the fees generally.

DR. LEE: I should hope that whatever action is taken will be tentative; there may well be a nominal fee, but now that Dr. Shaw has become the Educational Director and has to get his initial experience, more information will come later. There may be quite a different situation in the next few months.

DR. SLOAN: There should be further consideration given to the size of these courses. Let us not make a huge meeting out of a postgraduate course.

. . . On motion by Dr. Sloan, seconded and adopted, it was RESOLVED, that the question of nominal fees, or other fees, for postgraduate courses be left to the Executive Secretary and the Educational Director, under the direction of the Committee on Educational Policy. . . .

PRESIDENT IRONS: May we have the report of the Committee on Post-War Planning for Medical Service, Dr. George Morris Piersol, Chairman.

DR. PIERSOL: The Committee met yesterday at 6:00 p.m., with the Educational Director. You will recall a letter was sent to the Regents and Governors, asking them to submit data and information in regard to various available appointments, residencies, etc. This letter brought little results. Many answers were received, but few facilities are available. The demand for residencies and postgraduate training on the part of returning veteran members of the College far exceeds any available facilities.

Information collected by the Bureau of Information of the American Medical Association and cataloged by that Bureau according to counties throughout the country has been made available by the various State and County medical societies, and all Reserve Medical Officers on active duty have been advised. The College is not in a position to operate a placement service, and has been unable to guarantee any adequate amount of information to help any large proportion of the returning veteran members of the College. The best we can do is to refer these individuals to the Bureau of Information of the American Medical Association.

The Committee was in favor of circularizing deans of medical schools and postgraduate schools to obtain further information in planning a broad educational policy for the College. At present our activities are largely confined to carrying on our graduate courses.

. . . On motion by Dr. James E. Paullin, seconded and carried, the above report was adopted. . . .

PRESIDENT IRONS: May we have a report from the American Board of Internal Medicine? In the absence of the Chairman, Dr. Reginald Fitz, we will hear from Dr. James J. Waring.

DR. WARING: My report has been prepared by the very active and very efficient Secretary-Treasurer, Dr. William A. Werrell, of Madison.

Total receipts, from January 1 to October 31, 1945, are $16,000.00, which, with a holdover balance of about $3,000.00 amounts, in round figures, to $19,000.00 on deposit as of October 31, 1945. Disbursements to this date, October 31, 1945, $13,800.00, leaving a balance of about $5,200.00. Summary of the funds in hand include $40,000.00 in U. S. Savings Bonds and $7,000.00 in savings accounts in three different banks, with a balance on deposit in the Madison Trust Company, amounting to a total, as of October 31, 1945, of $57,000.00.

The total number of physicians certified, with special oral examinations conducted by Colonel William S. Middleton in the European Theater, 37; additional certifications in this country, May 22, June 8 and June 13, bring the total up to 303 certified by examination; 12 were certified without examination; total certifications, 315. Cer-

tifications in the sub-specialties: Allergy, 5; Cardiovascular Diseases, 13; Gastro-enterology, 9; in the sub-specialties without examination, 4; total certifications in the sub-specialties include 5 in Allergy, 13 in Cardiovascular Diseases, 12 in Gastro-enterology, 12 in Tuberculosis. Written examination data: February 19, 1945, 168 passed and 43 failed; 9 papers are not yet graded; grand total, 220. Written examinations held October 15, 1945: approximately 302 took the examination, but papers are not yet graded. The oral examinations scheduled to be held in San Francisco in the autumn had to be cancelled, because no hotel accommodations were available due to the arrival of the Pacific Fleet.

Dr. Werrell points out, in regard to the financial report, that the surplus is more apparent than real, because there is going to be a total of 407 candidates eligible to take the oral examinations in 1946, and this will be an expensive program. Dr. Werrell has also included herewith a spot map, showing the number of candidates and their locations over the country, eligible for the first, second and third oral examinations.

. . . On motion by Dr. David P. Barr, seconded and carried, the report was adopted. . . .

PRESIDENT IRONS: I would like to commend again Dr. Werrell, who is a most efficient operating secretary of whom we are all very appreciative.

Next will be the report of the Committee on Finance, Dr. Charles F. Tenney, Chairman.

DR. TENNEY: The Finance Committee met yesterday afternoon and reviewed in detail the operating statements prepared by the Executive Secretary for the year 1945, with estimations for November and December. A copy of these statements and comparisons are placed in your hands. You will find that the College operated below the budgets approved by the Board of Regents, and you will also note that the income was greater than estimated a year ago. This was largely due to increased income from subscriptions and advertising in the ANNALS OF INTERNAL MEDICINE, and to additional Life Members.

The Committee likewise surveyed in detail the proposed budgets, copies of which are in your hands, and recommends to the Board of Regents their adoption, with the addition of a total of $500,00 on the Executive Secretary's budget to provide an honorarium to the Treasurer's secretary and an honorarium to the Executive Secretary's secretary, and an addition of $75.00 for honoraria to two secretarial assistants in the Acting Editor's Office.

The Finance Committee reviewed recommendations received from the investment counselors, Drexel & Co., and within authority already vested in the Committee by the Board of Regents, has taken appropriate action with regard to the General Fund Account. The Committee, however, desires to obtain the approval of the Board of Regents in the following transactions concerning securities and investments in the Endowment Fund; to wit: authorization to proceed as follows:

(1) To invest approximately $3,800.00 of the Endowment Fund surplus cash in securities to be selected from later recommendations of the investment counselors;

(2) To sell $5,000.00 Great Northern Railway Company Bonds and $5,000.00 Pennsylvania Railroad Company Bonds, as recommended by the investment counselors, and to re-invest the proceeds for the Endowment Fund in acceptable securities later to be recommended by the investment counselors. These particular bonds were purchased at 89.27 and 100.26, respectively, and their present market prices are 121 1/8 and 126, respectively. It should be recorded that the investment counselors have already made recommendations for the investment of these funds, which, in the opinion of the Finance Committee, after careful consideration, are not wholly acceptable, and the Committee, therefore, is requesting other recommendations.

. . . On motion by Dr. Walter W. Palmer, seconded and regularly carried, the above report was adopted and approved. . . .

DR. WARING: In my report on the American Board of Internal Medicine, I referred rather casually to the oral examinations conducted by Colonel Middleton in the European Theater. Colonel Middleton's contribution was a most important one for the prestige of this organization and meant a great deal in the way of convenience and accommodation to the men individually concerned. I think more adequate recognition of that should have been made in my report.

PRESIDENT IRONS: In that connection, it has already been reported to the Board that the Board of Internal Medicine received very active coöperation from the Surgeon General, and that written examinations were held all over the world—North Africa, Australia, India and in other places, as well as in almost all of the larger military centers in this country. The holding of these examinations has been a very definite morale builder for a great many Medical Officers. They felt that everything they had done up to date had not all gone to waste. In the case of the oral examinations, however, in some other localities, we had no member of the American Board available, and it was felt that the Board could not delegate oral examinations to anyone, unless such examinations could be carried out under the medical direction of a member of the Board. That is not in disrespect of the ability of other Medical Officers who might conduct such examinations, but the Board had a definite responsibility that could not be delegated to others. Colonel Middleton was uniquely situated, and he did a most commendable job.

Next is the report of the Treasurer, Dr. William D. Stroud.

DR. STROUD: The Treasurer's report is supplementary to the report of the finance Committee the Board has already received. At the conclusion of the year, the accounts of the College will be verified by a public accountant, final financial reports prepared and presented to the Board of Regents.

It has probably already been drawn to your attention, through the financial statements already presented, that during 1945 certain appropriations were not used, because of restrictions due to the War. Referred to are the Regional Meetings of the College, which were curtailed by ODT regulations, and appropriation for a joint meeting of the Regents, Governors, and a few other minor items. Obviously, the appropriation for the Educational Director was not intended to be expended in its entirety in 1945, because it was clearly understood that the office would be established later in the year. The surplus anticipated for December 31, 1945, a grand total of approximately $39,000.00, is very much greater than was anticipated a year ago, but $15,000.00 of this belongs to the Endowment Fund and may not be expended, and the balance is the result of curtailment of activities occasioned by War restrictions.

The finances of the College are in wholly satisfactory condition, and we may look forward to increased income in the future. It seems appropriate that the Board of Regents authorize the extension of certain activities as an immediate post-war program, and that we draw moderately upon the Surplus Account of the College set up in previous years. This should not, however, be a precedent for continued overdrawing of the current income in years to come, for reasons that are obvious to all.

A survey of the College portfolio reveals that the Book Value of all holdings on November 7, 1945, was $317,511.12, whereas the Cash Value on that date was $354,083.75, showing an appreciation of $36,572.63. Our current yield on securities in the Endowment Account is 3.05%, and on the General Account 3.77%, or an average for the entire investment account of 3.36%. Our highest rate of income is from preferred stocks, 4.03%; on common stocks, the rate is 3.71% and on bonds, 2.93%. The College already holds in its portfolio $117,400.00 in United States Savings Bonds, on which the income is 2½%; this, naturally, has the effect of lowering materially the average rate of income.

We consider the services of our investment counselors, Drexel & Co., efficient and wholly satisfactory.

. . . On motion by Dr. George Morris Piersol, seconded and carried, the report of the Treasurer was adopted. . . .

PRESIDENT IRONS: We are faced with some very large and difficult problems in the matter of re-education assistance to returning Medical Officers, members of the College, and I would feel very much in favor of all measures possible for the continuing support of the College in this most important program. I think, however, we must be cautious in over-expending our surplus. There will come a time when the College will be very glad that it has been able to build up as large a surplus, or even a larger one, because when you go down the street with nothing in your pocket you are very likely to accept almost any kind of a proposition to get a bite to eat, whereas if you have money in your pocket your moral sense is very much more to the fore. Then you can throw out your chest. I am impressed with the importance of maintaining and building up a substantial reserve in the College. I say that because there is a tendency now and then to get emotional, quite properly so, but our emotions sometimes override our judgment in the expenditure of funds.

We have now concluded the Committee reports on the agenda. Dr. Meakins, will you elaborate on your all-American problem?

DR. JONATHAN C. MEAKINS: Mr. Chairman, I feel that in the years to come the eyes of many people will turn to North America for medical education, and we are restricted as to whom we may take in as Fellows, or who may be eligible as Fellows. I am wondering if a situation might arise like this: a man came from Australia, took the examinations of the Board of Internal Medicine and then sought to become a member of the College. The present policy of the College is to exclude physicians who are not bonafide citizens of some North American Country. The man I am speaking about might establish residency in this Country for some time, he might become an Associate and then return to Australia. Would he then be ineligible, no matter how good he be, to become a Fellow? In other words, I feel personally that the American College of Physicians, on account of the War, and our members being scattered all over the globe, has made a very distinguished name for itself. I believe men in other Countries would like to become Fellows.

PRESIDENT IRONS: This is an important matter. There is much to be said on either side. Possibly we might consider honorary Fellowships, or something similar thereto, which would not imply supervision, or too much responsibility, for the man who had been so admitted.

MR. LOVELAND: It is not officially written into the By-Laws of the College that only citizens of North America shall be admtited to the College, but it has been a policy of the Board of Regents and the Credentials Committee to discourage the admission to the College of physicians who are not citizens of this Continent, or who neither speak nor read English. Such a person would not be able to participate in our meetings, to read our journal or to give or receive the usual benefits of membership. The only value of his membership to him would be the use of the designation "F.A.C.P." Only yesterday there was a candidate from Brazil, who was sponsored by some of our New York Fellows, but election was denied, because of this previous principle adopted by the Board of Regents. If we were to extend College membership beyond North America, the By-Laws would have to be changed in those sections affecting the method or machinery of admission. A candidate must be proposed and seconded by Fellows of the College and endorsed by the College Governor for his territory. Naturally, we have no Governors outside of North America and our dependencies.

DR. PAULLIN: There is no provision for honorary members.

DR. WARING: I am interested in this matter, and I am quite in favor of extending College membership in some manner which would have to be seriously weighed by the Board of Regents, the Officers and the Credentials Committee, but I think there is a definite movement in the way of our extending the knowledge of what the American

medical profession is doing further and further to the South. For instance, the American Review of Tuberculosis, which has a very fine record and reputation throughout the English-speaking world, now publishes a summary of its articles in Spanish, as well as in English. There is another organization that has vigorously attempted to extend its membership south of the border. I mention this only to indicate there is definitely a tendency to try to bring physicians in Central and South American Countries into the sphere of American medical influence, and I think it is not a bad idea in this age when co-operation with other Countries is vitally important to our peace and future prosperity.

PRESIDENT IRONS: This question may be referred to the Public Relations Committee as a matter for report at the next meeting of the Board.

. . . On motion by Dr. David P. Barr, seconded and carried, the matter was so referred. . . .

PRESIDENT IRONS: Before luncheon we might discuss a few special problems and topics. Mr. Loveland, will you present the matter concerning Masterships?

MR. LOVELAND: Mr. President, in past years, as you know, the College has sporadically conferred a few Masterships. There has been no system in particular. These Masterships have been conferred primarily in appreciation and recognition of some great service, or services, to the College. We have had a good many such men, but we have recognized but few. It has occurred to me often, especially this past year, that there have been certain men who have in years gone by, and for many years, performed signal service who deeply merit recognition of their great contributions to the College. I haven't any prepared list, but I have already suggested to Dr. Irons that there should be a committee or agency in the College that would periodically review the question of recognition by Mastership of Fellows who have made the most worthy contributions to the College during the past many years, and who heretofore have not been recognized. I believe it a mistake to let these men go unnoticed until infirmities of body or mind would make it questionable whether Masterships should then be conferred. I have in mind one man who through two decades made great contributions to the College and who today is wholly disabled and is retired from practice, yet who should have been recognized long ago. There are other men whose contributions to this College are recognized by all men who are still active, to whom a Mastership would be a small recompense for their outstanding work in the College and their position in American Medicine.

. . . President Irons, in the absence of further discussion of the subject, passed on to a discussion of the policy of the College with regard to continuation of Regional Meetings. . . .

MR. LOVELAND: During the War, as you all know, the Regional Meetings held throughout the Country were the means of keeping the College active and alive in a real way. Members liked these Regional Meetings; the Governors organized fine programs, and the programs improved with experience. There may be a popular demand for continuing Regional Meetings regardless of our return to the Annual Session of the College. Before the War, the Regional Meetings were largely State Meetings, conducted for a single State. During the War, they became multi-State meetings, with from three to seven States combining. Regional Meetings, of course, cost money, and there is no financial return from exhibits. To continue this program as it has been conducted in the past year would cost at least $7,500.00 a year. There is no such appropriation on the budget for 1946. The Executive Office ought to have the advice of the Regents concerning the policy for the future, when a Governor or a group of Governors inquire about organizing future Regional Meetings.

PRESIDENT IRONS: The Chair has felt that the development of Regional Meetings, necessitated in part by the War and our failure to be able to hold the general meetings, has been one of the great benefits the College got out of the War. These Regional

Meetings have been tremendously helpful in maintaining interest in the College, and certainly they could be continued and developed further.

DR. STROUD: I have heard some discussion of this subject, and the point has been raised whether, if Regional Meetings be continued or extended, they would not directly affect the attendance at the general Annual Meetings. It seems to me the Regional Meetings will stimulate rather than detract from the Annual Session.

PRESIDENT IRONS: Nowadays we would not object if the Annual Sessions were a little smaller.

DR. PIERSOL: How much liability should the College assume for these meetings?

PRESIDENT IRONS: Perhaps they could be almost self-supporting?

MR. LOVELAND: They have not been self-supporting, because the College must publish programs, furnish postage, carry on a large amount of correspondence and bear local expenses. Not one of the Regional Meetings has been conducted without a deficit. In fact, the College agreed to meet deficits up to $250.00, but in some instances that has not been anywhere near adequate. The program committee of Regional Meetings has often wanted to invite distinguished guests, whose travel expenses must be met. Furthermore, these Regional Meetings cannot be as wholly under the direction of the Executive Office as is true of the Annual Sessions. More responsibility must be delegated to the Governors conducting the meetings.

PRESIDENT IRONS: Even at that, I should think the investment would be a good one.

DR. SLOAN: The Executive Offices might take a broader responsibility for these Regional Meetings, and more effectively thereby reduce the expense. Our experience in the past years will show where losses arose, and with care and direction to the General Chairman the expense could be reduced to a minimum. I would like to see the Regional Meetings kept up, perhaps, at a time of year not near that of the Annual Session. They will prove of real service to the College.

DR. PAULLIN: Could we provide $5,000.00 in the budget for that expense?

MR. LOVELAND: For 1946 we are already drawing upon the surplus from former years by approximately $20,000.00. That is because of an extended program for our educational department and the appointment of an Educational Director.

DR. PAULLIN: Could this $5,000.00 be absorbed in the educational program?

MR. LOVELAND: A part of it could, perhaps. On our 1946 budget for the Educational Director there appears an item of $2,500.00 for Postgraduate Courses. I believe the courses could be managed so that the cost to the College would not be that much. I am frank to say that I question the propriety of expending the tuition fees in the manner that some of the directors do.

DR. BARR: In the estimate for expenses and income for 1946, the budgets contain no item for income from commercial exhibits.

MR. LOVELAND: That matter was discussed in the Finance Committee meeting. In the first place, the Board of Regents had not previously directed that there would be an Annual Session, and we had not prepared a budget therefor. However, the income from the exhibits, if we resume the Annual Session in a large eastern center, should be adequate to pay the expenses of the meeting. There was discussion of this in the Finance Committee; a budget was not prepared; it was decided that if the Board of Regents authorize an Annual Session, that budgetary provisions for expenses should be made out of estimated income from the exhibits. I believe that this can be done. Our experience before the War was that our annual meetings cost approximately $13,000.00 and that our exhibits produced a net income varying from $12,000.00 to $14,000.00. However, when we met in St. Paul in 1942 there was a deficit of $3,000.00 on the annual meeting, but that was due to the location and the reduced size of the Technical Exhibit.

DR. CHARLES T. STONE: It seems to me that we ought not to abandon the Regional Meetings entirely in 1946, for the simple reason that even though the Annual Session

is held, the difficulties in transportation and hotels will considerably reduce our attendance, and those who cannot come to the annual meeting will want to attend some Regional Meeting later on. Isn't it a part of our responsibility to give these members some sort of a meeting in the area in which they live? It occurs to me, in connection with the expense of Regional Meetings, that it might be possible to have a nominal registration fee that would largely take care of the expense. I think the Finance Committee, of which I am a member, probably would be unwilling to dip into the permanent funds any more than already provided in 1946.

PRESIDENT IRONS: The Chair understands from the tenor of the discussions that it would be the wish of the Regents to have the Executive Secretary continue to encourage Regional Meetings and in a tactful way to intimate that they shall be self-supporting, as far as possible.

DR. LEE: I think it would be of much importance to have some central control over these Regional Meetings, this central control to be depended upon for financial assistance as well as getting out their programs and the like. In the beginning I was somewhat skeptical about these Regional Meetings, but I have changed my mind. I think they are very valuable. On the other hand, there is always a tendency—and I have looked over some of the Regional Meetings—that local committees may go a little far and wide in getting some of their speakers and drifting toward substituting a local annual session for a Regional Meeting. The control the central office can establish is very important; guest speakers should come from the region and not from the country at large.

PRESIDENT IRONS: I have a report from Dr. Francis F. Borzell, who is unable to be present. The War-Time Graduate Medical Meetings will close as of December 31, 1945, and the physical equipment, files, etc., will be turned over to the College as a small gesture because of the courtesies extended to the Committee by the College in its headquarters and also for the personal services of the Executive Secretary. Furthermore, Dr. Borzell wishes to inform the Board that enough finances are on hand to complete the work, and that any balance will be distributed pro rata among the three organizations sponsoring the War-Time Graduate Medical Meetings. Dr. Borzell extends his personal appreciation to the Board of Regents.

. . . A motion to accept the report of Dr. Borzell, with deep appreciation for his services, as well as for those of Dr. Edward L. Bortz, was made by Dr. William D. Stroud, seconded and unanimously adopted. . . .

LUNCHEON RECESS

PRESIDENT IRONS: The next item on the agenda is the consideration of resumption of the Annual Session of the College. That involves whether or not we shall have such a Session and, if so, the place, date and General Chairman.

DR. PAULLIN: I move we have an Annual Session in the spring of 1946.

. . . Motion was seconded and adopted. . . .

PRESIDENT IRONS: Where shall the Annual Session be held?

DR. PAULLIN: I move we meet in Philadelphia, where we were to have met in 1943.

. . . Motion was seconded and regularly adopted. . . .

PRESIDENT IRONS: On what date shall the Session be held?

MR. LOVELAND: Dr. Piersol, I, and others, have investigated the dates when facilities will be open in Philadelphia. We have also taken into consideration the dates of other meetings, including that of the Philadelphia County Medical Society's Postgraduate Institute. Easter falls on the 21st of April. We should not want the meeting during the week preceding or immediately following Easter. The Association of American Physicians will meet in Atlantic City on May 28 and 29; the American Medical Association is expected to meet in San Francisco during July. While the College has never

met as late as May, we would like to have that possibility considered. Philadelphia is lovely in May. April is oftentimes a nice month and oftentimes it is not. It would be ideal, from the standpoint of weather, during May, and we might readily consider a date near enough to that of the Association of American Physicians, to enable those from distant points in the West to come East, attending both meetings during one trip. The particular weeks that are open for discussion and consideration are the week of April 29 and possibly the week of May 13, or May 20, the latter being the week immediately preceding the Association's meeting in Atlantic City.

. . . There was general discussion entered into by all. It was pointed out that the week of April 29 conflicts with the Postgraduate Institute of the Philadelphia County Medical Society's meeting, already scheduled. . . .

. . . On motion by Dr. James E. Paullin, seconded and carried, it was RESOLVED, that the time of the meeting be referred to the President, the Secretary-General and the Executive Secretary. . . .

DR. WARING: I would like to suggest to the Committee on Postgraduate Courses that they consider the advisability of the sequential arrangement of local Postgraduate Courses and the Annual Meeting. In other words, men coming from a distance might be glad indeed to attend both a College Postgraduate Course in this area and also the Annual Meeting.

PRESIDENT IRONS: Whom do you suggest as the General Chairman of the Philadelphia Annual Session?

DR. PAULLIN: The same one who was elected before to be the General Chairman, had we held our meeting here in 1943, Dr. George Morris Piersol.

PRESIDENT IRONS: There appears to be a general feeling among the Regents that Dr. George Morris Piersol shall be asked to continue his work as General Chairman.

DR. PIERSOL: I shall be very glad to serve.

PRESIDENT IRONS: Next, may we discuss the nature of this meeting? What shall we do with regard to its general outlines? Shall we hold a Victory Convocation?

MR. LOVELAND: From the outbreak of the War, I think we have emphasized that when the War is over and we can resume our Annual Meetings, the Convocation for the induction of Fellows shall be organized as an especially impressive occasion. There will probably be a thousand Fellows to be inducted, and it is hoped that the great majority can be present. We thought it appropriate to call the next Convocation the "Victory Convocation."

PRESIDENT IRONS: Resuming the Annual Sessions will also take care of the election and installation of new Officers, Regents and Governors, which will take place in accordance with provisions of the Constitution and By-Laws.

We should authorize a meeting of the Committee on Credentials about one month in advance of the Annual Session, so that most of the Committee's work can be concluded in advance.

Are there any other items that should come before the Board at this time.

DR. PAULLIN: Mr. Chairman, before we adjourn, I think the Board of Regents ought to extend to Mr. Loveland a vote of thanks for what he has done and for the untiring effort he and his staff have made during these last years. They have been very unselfish, and we should recognize it by extending a vote of thanks.

. . . The Regents all rose in an expression of thanks. . . .

. . . The meeting *adjourned* at 1:45 p.m. . . .

Attest: E. R. LOVELAND,
Secretary

OBITUARIES

DR. JOHN MINOR BLACKFORD

Dr. John Minor Blackford died September 12, 1945 at the Virginia Mason Hospital in Seattle, Washington. Dr. Blackford became ill Saturday, September 8 on arriving home from a trip to Alaska.

Son of Launcelot and Eliza Blackford, he was born February 1, 1887 at Alexandria, Virginia. Educated in that State, he received his medical degree in 1910 from the University of Virginia and served his interneship at the University of Virginia Hospital. He served on the staff of the Mayo Clinic at Rochester, Minnesota from 1911 until 1917 after which he came to Seattle, Washington.

In 1918, with the late Drs. James Tate Mason and Maurice F. Dwyer, Dr. Blackford helped found the Mason Clinic and later, in association with them and others, built the Virginia Mason Hospital. His imagination and ability as an organizer were major factors in the later enlargement of the Hospital and improvement of its services. To the institutions of the Virginia Mason Hospital and the Mason Clinic, he gave liberally of his energy and enthusiasm up to the time of his death.

Dr. Blackford was the author of many articles in medical and scientific journals and was a member of the Washington State Medical Association, the King County Medical Society, American Medical Association, American Gastroenterological Association, the North Pacific Society of Internal Medicine, Fellow of the American College of Physicians, and Diplomate of the American Board of Internal Medicine.

In January, 1927, Dr. Blackford, Dr. George F. Strong, and Dr. Frederick Epplen met in Spokane, Washington and conceived the idea of an association of internists in the Pacific Northwest. At an organization meeting in Seattle, April 24, 1927, these three men selected a group of 19 internists, including themselves, as founders of the North Pacific Society of Internal Medicine.

Surviving Dr. Blackford are his widow, Mrs. Elizabeth Mann Blackford at the family home, 4318 55th Avenue N.E.; a son, Commander William Mann Blackford, Executive Officer at the Great Lakes Naval Training Station; two daughters, Mrs. J. Newton Morris and Mrs. Marvin McClatchey, Jr., of Seattle, and four grandsons.

His outstanding medical ability and judgment, which early placed him among the leaders of the medical profession in the Pacific Northwest; his observations and contributions to medical literature; his sterling character, which attracted the support of his medical confreres and business associates, are apparent. His ideal family life, his association of over twenty-five years in a professional partnership which notoriously requires a maximum of fairness and the ability to compromise, his kindliness of character and the warmth of his personality, produced in professional contacts a large pro-

portion of warm personal friends. Rarely indeed can a man in any station of life lay down his burdens at his time of life and have the void which his passing creates so completely filled with the loving memories of his family and the appreciation of his friends. To each of his associates and to his patients his death is a personal loss.

E. G. BANNICK, M.D., F.A.C.P.,
Acting Governor for Washington

DR. TOM LOWRY

In preparing this obituary of Dr. Tom Lowry, M.D., F.A.C.P., Dean of the University of Oklahoma School of Medicine, it is quite unnecessary to speak in laudatory terms to those who knew him. Dr. Lowry was exceptionally naive in making friends and in keeping them. He was a man among men. Respected because of his ability in his chosen profession, his sterling qualities as a man, about whom no one could say aught but good concerning his character, friendly manner, and religious background. Endowed with an unusually fine voice, he and his brother responded generously in singing alone or with a quartet. Strong of muscle and fleet of foot, these brothers were known for their prowess in athletics. Their versatility was remarkable.

In writing of Dr. Tom, it would be amiss not to speak also of his identical twin brother, Dr. Dick, who succumbed in the same dramatic way four years ago. Two brothers could not have been more alike in stature, looks and accomplishment. His father, his older brother, and his twin brother all were victims of coronary occlusions. Dr. Tom often spoke of his impending doom, but his fortitude and equanimity were marvelous. With this in mind, he gave up a large and lucrative practice, following his brother's death, and accepted the Deanship of the University of Oklahoma School of Medicine. Previously he had been occupying the Chair of Clinical Medicine. The morning after his election as Dean he was stricken with a coronary episode which laid him up for several months, and thereafter he was able to devote only a few hours a day to the Deanship.

Dr. Tom lived in Oklahoma most of his life; he graduated from the Oklahoma University at Norman with a B.S. degree in 1914, and an M.D., 1916. Having acted as councillor for his district in the Oklahoma State Medical Association, the horizon of his activities was broad, enabling him to be of great value to the betterment of medicine. He served as a Captain in World War I and was with the 24th Evacuation Hospital in France. Thereafter, in 1924, he pursued a course at the Colorado School of Tuberculosis.

He was a member of his County and State Medical Societies and a Fellow of the American Medical Association. He had been a Fellow of the American College of Physicians since 1929. He was certified by the Ameri-

can Board of Internal Medicine; a member of the Methodist Church; a Rotarian; a member of the Phi Beta Pi Medical Fraternity; a member of the Phi Beta Kappa National Scholastic Fraternity; a member of Phi Mu Alpha Biology Group; Pe-et, because of being the outstanding freshman at the University; and he received the Litzeiser Medal as an outstanding senior.

Dr. Tom was stricken with the second coronary episode after a night call to his aged mother and died the same day, December 11, 1945. His remains were interred in Memorial Park Cemetery among a large concourse of friends. He is survived by his mother, wife, and three daughters: Mrs. Robert Wallace King, a granddaughter Sheryl Lou King, of New York City; Miss Jean Lowry, a student at Columbia University; and Miss Elizabeth Ann Lowry, at the University of Oklahoma.

LEA A. RIELY, M.D., F.A.C.P.,
Governor for Oklahoma

COLONEL HARLEY JAMES HALLETT, (MC), U. S. A. (RET'D)

Colonel Harley James Hallett, F.A.C.P., Lake Wales, Florida, died suddenly on December 11, 1945, of coronary occlusion.

Colonel Hallett was born at McLean, Illinois, September 16, 1880. He graduated in medicine from the Jefferson Medical College of Philadelphia in 1905 and early entered the Medical Corps of the United States Army. For many years he was Chief of the Medical Service at the Army and Navy General Hospital at Hot Springs, Arkansas. He attained the rank of Colonel in March, 1937. He had fulfilled numerous assignments in the Army including Post Surgeon and Commanding Officer at the Station Hospital, Fort Devons, Massachusetts, and Post Surgeon, Fort Kamehameha, Honolulu, T. H. He retired from active duty on November 30, 1940, and for the past few years had been residing at Lake Wales, Florida.

Colonel Hallett was a member of the American Medical Association and had been a Fellow of the American College of Physicians since 1930. He was a man of splendid professional qualifications and his passing is recorded with deep regret. He is survived by his wife, Mrs. Helen M. Hallett, Lake Wales, Florida.

DR. BENJAMIN WARREN BLACK

Benjamin Warren Black, M.D., F.A.C.P., passed away at his home in Oakland, California on December 1, 1945. Born in Fillmore City, Utah, May 21, 1887, Dr. Black spent his early life in Utah and received his premedical training at the University of Utah; also at the University of Chicago, receiving his M.D. degree in 1916 from the Medico-Chirurgical College of Philadelphia. He had an active and interesting career, serving in World War I in the United States Army from 1917 to 1919. He was

Regimental Surgeon with the rank of Major, serving with the 157th Infantry. At the time of his death he was a Lt. Colonel in the Medical Reserve on inactive status. From 1920 to 1921 Dr. Black was with the U. S. Public Health Service. From 1924 to 1926 he was Executive Officer with the U. S. Veterans Bureau, and Medical Director of the U. S. Veterans Bureau from 1926 to 1928. From 1928 to the time of his death, he served as Medical Director of Alameda County; also serving as medical-legal advisor to the District Attorney's office, Alameda County. He was a member of the Board of Directors of the First Federal Savings and Loan Association, of Oakland. Dr. Black was President, 1940 to 1941, of the Oakland Forum. He was President in 1940 of the American Hospital Association; Director in 1940 of the Western Institute of Hospital Administration. He was a Fellow and former Vice-President of the American College of Hospital Administrators. He was a member of the American Association for the Advancement of Science, Association of Military Surgeons of the United States, the California Academy of Medicine, Fellow of the American Psychiatric Association, and American Medical Association. He became a Fellow of the American College of Physicians in 1927.

Dr. Black contributed numerous articles to the medical literature, being interested chiefly in hospital administration and psychiatry. He was an active and very interested Fellow of the College. His civic activities included the following: Trustee of the Kiwanis International; a thirty-third degree Mason, including Scottish Rite (Master 1940) and Shrine; member of the Commonwealth Club and Claremont Country Club. One of his chief means of recreation was golf.

Dr. Black is survived by his widow, Mrs. Jean Black, and a daughter, Margaret Black Kockritz; also a son, Benjamin Marden Black, M.D., a surgeon at the Mayo Foundation in Rochester, Minnesota.

Dr. Black held a very important hospital administrative position in Alameda County. His special ability as an organizer did much to build up the Alameda County hospitals. He was always very much interested in younger doctors, great numbers having passed under his influence as a hospital administrator. His advice and assistance helped many to secure a start after leaving hospital training.

ERNEST H. FALCONER, M.D., F.A.C.P.,
Governor for Northern California

DR. LAWRENCE JOSEPH RIGNEY

Lawrence Joseph Rigney, M.D., F.A.C.P., Wilmington, Del., died November 28, 1945, in the St. Francis Hospital after a long illness.

He was born February 19, 1890; received his pre-medical training at the University of Delaware; M.D., 1920, University of Maryland School of Medicine; was Chief Resident Physician of the Bayview Hospital in

Baltimore; postgraduate work on numerous occasions at the University of Pennsylvania; served as Instructor in Medicine, 1930–1941, in the University of Pennsylvania School of Medicine. Since 1933, Dr. Rigney had been Chief of Medicine, Gastro-intestinal Clinic, St. Francis Hospital, Wilmington, and a member of the Staff of the Delaware Hospital. He was the author of several published papers, and formerly served as Vice-President of the New Castle County Medical Society. He was a member of the Delaware State Medical Society and the Delaware Academy of Medicine; a Fellow of the American Medical Association, and had been a Fellow of the American College of Physicians since 1941.

LEWIS B. FLINN, M.D., F.A.C.P.,
Governor for Delaware

DR. MILLS STURTEVANT

Dr. Mills Sturtevant, F.A.C.P., died on October 29, 1945, of pneumonia.

He was born in Whitefield, New Hampshire, in 1882; attended Manchester, New Hampshire, public schools; A.B., 1904, Dartmouth College; M.D., 1908, Columbia University College of Physicians and Surgeons; Interne, 1908–1910, Bellevue Hospital; Resident Physician, 1910–1913, Louisa Minturn Hospital; Visiting Physician, 1913–1919, and Chairman of Board of Trustees, 1918, of same institution; Assistant Visiting Physician, 1913–1918, Willard Parker Hospital; Visiting Physician, 1915–1917, Central and Neurological Hospital; for many years Visiting Physician in charge of gastro-enterology, Bellevue Hospital, and in later years Consulting Physician at Bellevue Hospital; Professor of Clinical Medicine, New York University College of Medicine; member of his County and State Medical Societies, the Harvard Society, the Quiz Medical Society, Manhattan Medical Society, Bellevue Alumni Society, and American Gastro-enterological Society; Fellow, New York Academy of Medicine, American Medical Association, and American College of Physicians, the latter since 1920; author of numerous published papers; Diplomate, American Board of Internal Medicine.

Dr. Sturtevant had been an active and enthusiastic Fellow of the College since 1920 and had been a Life Member since 1937.

ASA L. LINCOLN, M.D., F.A.C.P.,
Governor for Eastern New York